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The Impact of Surgery on Balance, Gait, Upper limb Dexterity and Dizziness in Patients with Posterior Fossa Tumours

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The Impact of Surgery on Balance, Gait, Upper limb Dexterity and Dizziness in Patients with Posterior Fossa Tumours

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A Thesis submitted in fulfilment of the requirements for the Degree of Masters of Science by Research.

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Candidate Thesis Declaration

I declare that this thesis, which I submit to RCSI for examination in consideration of the award of a higher degree by research, is my own personal effort. Where any of the content presented is the result of input or data from a related collaborative research programme this is duly acknowledged in the text such that it is possible to ascertain how much of the work is my own. I have not already obtained a degree in RCSI or elsewhere on the basis of this work. Furthermore, I took reasonable care to ensure that the work is original, and, to the best of my knowledge, does not breach copyright law, and has not been taken from other sources except where such work has been cited and acknowledged within the text.

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List of Abbreviations

ACPP	Atypical Choroid Plexus Papilloma
ADL	Activities of Daily Living
AP	Antero-posterior
AT	Adaption Test
BBB	Blood Brain Barrier
BT	Brain Tumour
CARE	Case Reports
CDP	Computerized Dynamic Posturography
CNS	Central Nervous System
COG	Centre of Gravity
CP	Cerebello-Pontine
CPT	Choroid Plexus Tumour
CSF	Cerebro-spinal Fluid
CT	Computerized Tomography
CXT	Cerebrotendinous Xanthomatosis
DHI	Dizziness Handicap Inventory
ET	Equitest
EVD	Extra-ventricular Drain
FIM	Functional Independence Measure
FITT	Frequency, Intensity, Time and Type
GBM	Glioblastoma Multiforme
GCS	Glasgow Coma Scale
GP	General Practitioner
HIV	Human Immunodeficiency Virus
HRQOL	Health Related Quality of Life

HSE	Health Service Executive
IARC	International Agency for Research on Cancer
ICC	Intraclass Correlation Co-efficient
ICF	International Classification of Functioning, Disability and Health
ICP	Intra-cranial Pressure
ITU	Intensive Therapy Unit
LASA	Linear Analogue Scale Assessment
LOS	Length of Stay
MCT	Motor Control Test
MDT	Multidisciplinary Team
METS	Metastases
MOOSE	Meta-analysis Of Observational Studies in Epidemiology
MRI	Magnetic Resonance Imaging
MS	Multiple Sclerosis
NCCP	National Cancer Control Programme
NCRI	National Cancer Registry of Ireland
NHPT	Nine Hole Peg Test
NIH	National Institute of Health
NRS	Numeric Rating Scale
PA	Pilocytic Astrocytoma
PACS	Picture Archiving and Communication System
PF	Posterior Fossa
PI	Principal Investigator
PNET	Primitive Neuroectodermal Tumours
QOL	Quality of Life
RCT	Randomized Controlled Trial

SD	Standard Deviation
SECS	Seconds
SEER	Surveillance, Epidemiology, and End Results
SOL	Space Occupying Lesion
SOT	Sensory Organisation Test
STROBE	Strengthening the Reporting of Observational studies in Epidemiology
TBI	Traumatic Brain Injury
TP	Time-point
TUG	Timed Up and Go
UK	United Kingdom
USA	United States of America
VAS	Visual Analogue Scale
VEGFA	Vascular endothelial growth factor A
VHL	Von Hippel-Lindau
WHO	World Health Organisation
WS	Walking Speed

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Summary

Introduction: Tumours of the posterior fossa of the cranium are associated with significant impairments, morbidity and mortality. Limited evidence is available in the adult population, of the potential impact a surgical intervention can have on function, in this tumour type. The rehabilitation practices utilised to treat the associated impairments have also received limited investigation.

Aims/Objectives: The primary aim of this research study was to characterise the impact of surgery on balance, gait, upper limb dexterity and dizziness in patients with posterior fossa tumours. Secondary aims of the study were to profile the demographic and tumour characteristics of the study participants.

Methods: This was a prospective cohort study, which recruited thirteen participants over an eighteen month period. A comprehensive testing battery was completed over four time-points, of six months duration, to categorise the impact of surgery. A systematic review of rehabilitation practices in the management of impairments, associated with posterior fossa tumours, was also completed.

Results: Thirteen participants, of mean age 48.8 ± 15.7, were recruited to the study. An improvement in the primary outcome, equilibrium and balance, was observed post-operatively, while surgical impact on gait speed, upper limb dexterity and dizziness resulted in negative consequences. Significant morbidity and mortality was associated with surgery in this population, impacting on data collection and analysis.

Conclusions and Implications: Surgical intervention for the presence of a tumour in the posterior fossa, resulted in a decrease in gait speed and upper limb dexterity, an increase in dizziness and improvement in balance, post-operatively. The most frequently occurring tumour type was metastases, indicating the high risk of mortality associated with a tumour of this region of the brain. The testing battery used in this research project provides the foundation for comprehensive assessment and treatment of this population of patients, in future care.

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Chapter 1: Introduction

1.1 Purpose of the Thesis

The purpose of this thesis was to quantify and detect changes in balance, gait, upper limb dexterity and dizziness in individuals with tumours of the posterior fossa, before and after a surgical intervention.

The posterior cranial fossa is a bony cavern at the rear of the skull that cradles the cerebellum, brainstem and fourth ventricle (Chadha et al., 2015). Tumours of this region of the brain remain very rare in adults but occur with increased frequency in the paediatric population. Almost 50% of paediatric brain tumours occur in the posterior fossa (Rasalkar et al., 2013), with only 15-20% of all adult brain tumours occurring in the posterior fossa (Lindsay and Bone, 2004). Although there is a discrepancy in incidence rates of posterior fossa tumours between adults and children, clinical presentation between adults and children is considered to be essentially similar (Levin, 2002).

Expansion of a tumour in the posterior fossa can occur at the expense of the normal cerebral tissues, and may result in brain stem or cerebellar dysfunction, blockage of the fourth ventricle and hydrocephalus (McMillan et al., 2009). Damage to the cerebellum has been revealed to cause a myriad of physical symptoms such as gait ataxia (Palliyath et al., 1998, Ilg et al., 2007), postural disorders (Marquer et al., 2014), balance deficits (Schoch et al., 2010), alterations in upper limb dexterity (Ada et al., 2009) and more recently, impaired cognition (Koziol et al., 2014). The brainstem plays a significant role in postural control and locomotion due to the presence of the vestibular, reticular and red nuclei, while also influencing arousal and awareness (Shumway-Cook and Woollacott, 2007).

The aim of management of a tumour in this region of the brain is ultimately to reduce the compressive impact of the tumour, relieve intra-cranial pressure and ultimately prevent progressing, neurological decline (Bullock et al., 2006). Several potential surgical procedures can be utilised to manage a tumour occurring in this region. Resection of posterior fossa tumours traditionally resulted in permanent bone removal, with a sub-occipital craniectomy, which improved tumour exposure but resulted in a higher associated surgical risk (Legnani et al., 2013). A craniotomy results in reinsertion of the bone flap post-surgically, allowing more protection of the cerebral tissues (Gnanalingham et al., 2002).

Once access to the tumour is obtained, a sample of the tissue can be collected by biopsy or a more aggressive approach involving resection of the tumour, either partially (sub-total) or fully (gross-total excision) (Valdes-Gorcia et al., 1998). Surgical techniques undertaken as a result of a lesion in this area of the brain are not solely concerned with identification and removal of the tumour. Given the proximity to the fourth ventricle, surgical procedures are often undertaken to manage hydrocephalus. Use of extra-ventricular drainage systems can be employed as temporary measures but ventriculostomy or permanent shunting may be required in certain cases to manage hydrocephalus in individuals with posterior fossa tumours (Mangubat et al., 2009).

The complex nature of the associated tissues, the evolving nature of the tumour and the potential for neurological impairments, poses a significant challenge to the multidisciplinary team, involved in care. The role of physiotherapy in the management of neuro-oncology patients is essential to maximise function, in conjunction with medical or surgical intervention. However, the available literature focusing on rehabilitation, specifically in patients with the diagnosis of a posterior fossa tumour, is limited.

1.2 Justification for the Thesis

While the incidence of primary and secondary brain tumours, has increased over the last several years (Deorah et al., 2006), tumours of the posterior fossa remain rare. The rarity of the condition is reflected in the lack and quality of available research in adult patients, with involvement of this area of the brain. While good quality evidence is available (Martin et al., 2009), focus has been placed on management of impairments as a consequence of varying pathologies. The complex role of the anatomical structures in this region of the brain, in the involvement of movement generation, movement timing and sequencing provides a challenge for therapists in their management of this complex cohort. No specific research has previously focused on impairments of balance, gait, upper limb dexterity and dizziness solely in an adult posterior fossa tumour population. This novel piece of research has the potential to supplement the existing knowledge base and assist therapists with future clinical decisions, involving this cohort of patients.

1.3 Structure of the Thesis

The thesis is divided into seven chapters, including the current chapter. Chapter two contains a literature review of cancer and brain tumour epidemiology, the anatomy of the posterior fossa and medical and surgical techniques employed in their management. Chapter three contains a general overview of rehabilitation in brain tumour populations and a systematic review of rehabilitation practices in the management of patients with posterior fossa tumours. The review focuses on the impairments associated with a tumour of the posterior fossa and potential rehabilitation strategies employed to treat subsequent impairments. Chapter four outlines the methodology of a prospective cohort study which investigated the impact of a neurosurgical intervention on balance, gait, upper limb dexterity and dizziness in a cohort of patients with posterior fossa tumours. Chapter five details and outlines the results of the cohort study, while chapter six contains the discussion, outlining the potential clinical implications of the study. Chapter seven contains the study conclusion.

Chapter 2: Anatomy and Medical Management Literature Review

2.1 Introduction

This chapter of the thesis aims to provide context for the proposed study by providing an overview of the epidemiology of cancer, in particular cancer of the central nervous system (CNS). In addition, the anatomical function of the structures located within the posterior fossa will be described, as well as the impact that a tumour in this region and the associated medical and surgical interventions, may have on normal brain function. Chapter one of this thesis, has provided an introduction to these concepts and this chapter aims to provide a more in-depth review of the relevant literature.

2.2 Epidemiology of Cancer

2.2.1 Cancer Incidence

According to the International Agency for Research on Cancer (IARC), 14.1 million new cases of cancer diagnosis were made in 2012 worldwide (IARC Biennial Report, 2012-2013). This is a 10% increase in cancer incidence, when compared with 2008 figures (Ferlay et al., 2010). Cancer is the second leading cause of death in high income countries and the third leading cause of death in medium and low income countries. By 2030, the global burden is expected to grow to 21.7 million new cancer cases and 13 million cancer deaths, due to the growth and aging of the population (Bray et al., 2012). In 2008, the European Union had 2.45 million new cancer diagnoses (Luengo-Fernandez et al., 2013). More recent European data demonstrated 3.4 million new cancer cases, excluding non-melanoma skin cancers, in 2012 (Ferlay et al., 2013). Irish data on cancer incidence, as compiled by the National Cancer Registry, displayed an average of 18,500 invasive (excluding non-melanoma skin) cancers, were diagnosed annually between 2008 and 2010, equivalent to an incidence rate of 423 cases per 100,000 per year. Based on increases in population and an aging population, it is predicted that the incidence of cancer is set to increase by 81% for females and 108% for males in Ireland between the period of 2010 to 2040 (National Cancer Registry, Cancer Projections for Ireland 2015-2040, 2014). This projection anticipates an increase in all cancer types, for both sexes, with the exception of leukaemia in males in Ireland, by 2040.

The incidence of developing a primary brain tumour in 2004 was identified as 6.6 per 100,000, with the incidence of metastatic brain tumour estimated to vary between 8.3 per

100,000 to 11 per 100,000 (Barnholtz-Sloan et al., 2004) . The worldwide incidence of developing a primary malignant brain or CNS tumour in 2012 was 3.4 per 100,000 (IARC Biennial Report, 2012-2013). CNS cancer was the 15th most commonly occurring cancer in Ireland (Cancer in Ireland 2013: Annual Report of the National Cancer Registry, 2013).

2.2.2 Cancer Mortality

The American Cancer Society identified cancer as a cause of 7.6 million deaths worldwide in 2008. Recent trends have shown that fluctuations are occurring in the mortality rates associated with varying cancer types. In the USA, between 1998 and 2007, a downward trend in mortality rates was noted for seven of 15 of the most frequently occurring cancers. These cancers included brain tumours, stomach, colon and kidney cancer (Kohler et al., 2011). Based on data from the 28 member states of the European Union, cancer resulted in the death of 1.281 million people, equating to more than one quarter of all deaths (26.3%), in 2011 (Eurostat, 2014). This data also highlighted Ireland as one of only three countries, with the Netherlands and Slovenia, in 2011, with a greater than 30% mortality rate associated with a cancer diagnosis. Age related discrepancies in cancer mortality have also been highlighted in the data, with 40% associated cancer mortality in those under the age of 65 and less than 25% associated mortality in the over 65 age category (Eurostat, 2014).

Irish data, looking at cancer mortality trends from 1950 to 2002, identified brain and CNS cancer as the twelfth most common cause of cancer death in Ireland, for the period 1994-2001 (O'Lorcain et al., 2006). Survival prospects, based on EuroCare 3 data, associated with a CNS cancer diagnosis, are considered relatively poor, with a mean 5 year relative survival of 18% in both sexes, for the time-period of 1990-1994 (Sant et al., 2003). EuroCare 5 data (Sant et al., 2012), demonstrated a 5 year relative survival of 85%, for a benign CNS tumour diagnosis and 19.9% for a malignant CNS diagnosis. Differences between the datasets are evident due to the inclusion of benign tumour cases in the latter study. Data for the UK and Ireland revealed a 40% higher excess risk of death with a CNS tumour diagnosis, when compared with Northern European participants.

2.2.3 Cancer Expenditure and Costings

While the exact global cost of cancer treatment and management is unknown, it is estimated to cost hundreds of billions of dollars annually (American Cancer Society, 2012).

Prediction of true and accurate cancer expenditure incorporates both direct and indirect cancer expenses. Direct expenditure relates to the direct medical treatment of cancer sufferers and includes hospital admissions, rehabilitation and cancer drugs (Jayadevappa et al., 2005). Indirect expenditure predicts the global cost of secondary costs relating to cancer such as loss of work related productivity, increases in mortality and premature death (Brown et al., 2001). In a review of United States data, the annual cost of cancer care in America in 2012 was estimated to be $124.57 billion, with an anticipated increase in costs to $157.77 billion by 2020 (Mariotto et al., 2011). This represents a 27% increase in the provision of routine cancer care to the American population, by the year 2020. In Europe, based on 2009 statistics, the total economic cost of cancer was in excess of €126 billion. On comparison of the cancer related funding per citizen, between the USA and Europe, the USA spent $255 (€196) per person as compared with €102 per European citizen in 2008. The Irish per head of population spending on cancer was €139, which equates to 136% of the European average (Luengo-Fernandez et al., 2013). This incorporates the direct cost of healthcare and associated productivity losses due to morbidity and mortality (Luengo-Fernandez et al., 2013).

One quarter of the global burden of cancer is observed within Europe, while Europe contains only one ninth of the world's population (United Nations, 2010). However, it is not just the healthcare system that carries the burden of cancer management. In a report by the NCRI (Financial Impact of a Cancer Diagnosis, 2010) patients have been shown to experience a large degree of personal financial stresses due to changes in financial earnings, increased health related expenditure and inability to return to gainful employment impacting on future earnings. While exact figures are unavailable in the report, it provides insight into the cost of cancer at a personal level, in comparison to societal and epidemiological cost analysis.

Expenditure related to cancer type varied based on the location of the cancer and the stage of cancer progression. Brain, pancreas, ovary and oesophagus were identified as the cancer locations with the highest annual cost to manage in the first year of diagnosis (Mariotto et al., 2011). Treatment of brain tumours in the US in 2010 cost the American government $4.5 billion, with an estimated increase in the resources required to administer cancer care by 2020, rising to $6.8 billion. The projected increase in costs accommodates inflation and

changing trends in cancer incidence, prevalence and mortality over the ten year period (Mariotto et al., 2011).

The destructive capacity of cancer on society and individuals has been outlined. When cancer occurs within the CNS there are several additional factors that also need to be considered such as cognition, movement and higher executive functioning (Levisohn et al., 2000). The destructive nature of brain cancer is even more apparent in complex areas of the brain, such as those located within the posterior cranial fossa.

2.3 Anatomy of the Posterior Cranial Fossa

The human skull consists of three distinct anatomical regions; the anterior, middle and posterior cranial fossae. The posterior cranial fossa is a bony cavern located at the posterior aspect of the skull. This region of the skull provides a bony cradle to protect complex brain structures including the cerebellum, brainstem and fourth ventricle (Levin, 2002).

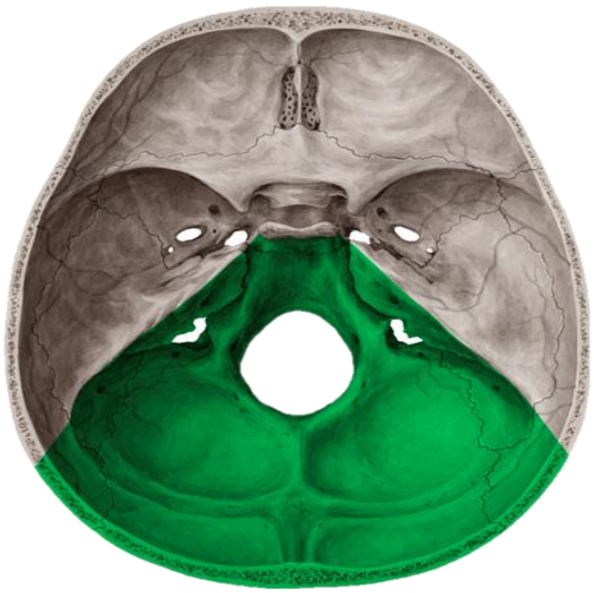


Figure 2a The posterior fossa of the skull

Ten of the twelve pairs of cranial nerves have a portion located within the posterior fossa (PF) (Matsushima et al., 1982). On sagittal MRI images the boundaries of the posterior fossa are made up superiorly of the tentorium, the anterior boundary, the clivus and the inferior boundary, the line joining the opisthion and basion (Chadha et al., 2015). The brain structures located superior to the tentorium, a sheath of dura, are classified as supra-tentorial and the structures inferior are classified as infra-tentorial. The complexity of the

brain structures located in the posterior fossa indicates the capacity for potential dysfunction with involvement of this area of the brain. The presence of a mass lesion within the infra-tentorium of the brain has been shown to be associated with compression and distortion of these complex structures. The compact nature of the PF results in an inability to accommodate increases in pressure, that could be caused by haemorrhages (Bullock et al., 2006), tumours (McMillan et al., 2009), hydrocephalus (El Ahmadieh et al., 2013) or mass effect (Jauss et al., 1999). Changes in volume or pressure within the supra-tentorial region of the brain also have the potential to increase pressure on the neural structures of the PF due to its rigid structure (Chadha et al., 2015).

2.4 Anatomy of the Cerebellum

The cerebellum constitutes approximately one-tenth of the cerebral volume and is connected directly and indirectly to a variety of cerebral structures including the brainstem, the spine and diverse cerebral subcortical and cortical regions (Roostaei et al., 2014). Within the posterior fossa, the cerebellum is located posterior to the brainstem and the fourth ventricle and is rostrally separated from the cerebrum by an extension of the dura matter called the tentorium cerebelli (Crossman and Neary, 2005). It is connected directly to the brainstem by three pairs of fibrous peduncles, known as the superior, middle and inferior peduncles, through which pass all afferent and efferent connections with the cerebrum. Gross makeup of the cerebellum is that of two hemispheres separated by the central vermis. Anatomically, the cerebellum consists of three lobes that are subdivided by two transverse fissures. The primary fissure divides the anterior and posterior lobe and the postero-lateral fissure separates the posterior and flocculonodular lobe (Roostaei et al., 2014).

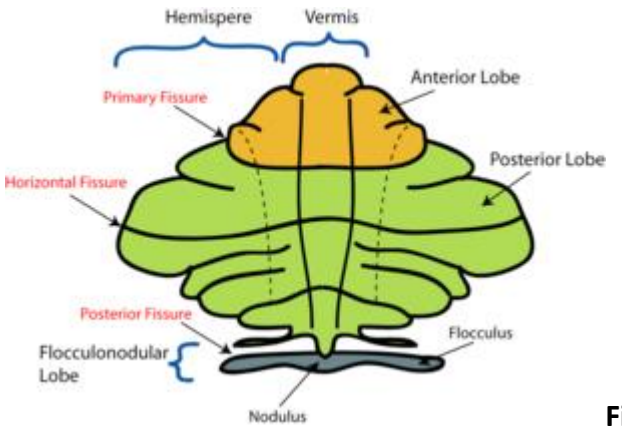


Figure 2b Structure of the cerebellum

Anatomical studies have shown that approximately 80% of all the brains neurones, in humans are located in the cerebellum (Herculano-Houzel, 2010), which highlights its complex computing capabilities. Four main types of neurones are located within the cerebellar cortex: granule cells, purkinje cells and the inhibitory Golgi cells and stellate/basket cells (Voogd and Glickstein, 1998), and are located within distinct histological layers in the cerebellar cortex. The outermost molecular layer is composed of the inhibitory stellate and basket cells and the dendritic arborisations of the purkinje cells that extend from the intermediate unicellular purkinje cell layer (Kirsch et al., 2012). The innermost layer of the cerebellar cortex, the granular layer, contains mossy fibres, granule cells, uni-polar brush cells and inhibitory golgi cells (Kirsch et al., 2012). Granule cells which are small round cells found within the granular layer of the cerebellar cortex, are the most frequently occurring cell of this region of the cerebellum and are believed to play a role in the modulation of motor output (Pinzon-Morales and Hirata, 2015).

The main afferent projections to the cerebellum arise from the spinal cord, inferior olivary nucleus, vestibular nuclei and the pons. The axons terminate in the cerebellar cortex and are excitatory in nature. The fibres originating in the inferior olivary nucleus give rise to climbing fibres, while all other afferents form mossy fibres. Mossy fibres terminate in the granular layer in synapse with the granule cells. In turn, the axons of the granule cells project to the superficial molecular layer producing two parallel fibres, which traverse the dendrites of the purkinje cells, which also extend into the molecular layer. The parallel fibres provide excitatory input to these dendrites. Climbing fibres also provide excitatory input to the purkinje cells. Both fibre types extend to the deep cerebellar nuclei that regulate cerebellar output (Crossman and Neary, 2005).

Four pairs of cerebellar nuclei are located within the white matter of the cerebellum; the fastigial, globose, emboliform and dentate nuclei. The dentate nucleus, the largest of the nuclei, was historically believed to project solely to the primary motor cortex of the cerebrum, however, recent studies have found that other portions of the nucleus also innervate occulomotor, prefrontal and posterior parietal areas (Dum and Strick, 2003).

2.5 Anatomy of the Fourth Ventricle

The fourth ventricle is a broad, tent-shaped midline cavity, located between the cerebellum and the brainstem (Rhoton, 2000). The fourth ventricle, the lateral ventricle, the third ventricle and the cerebral aqueduct comprises the ventricular system (Crossman and Neary, 2005). It is located ventral to the cerebellum, dorsal to the pons and medulla and medial to the cerebellar peduncles (Rhoton, 2000). Several of the cranial nerves are located within the floor of the fourth ventricle. The main function of the fourth ventricle is in the production and transport of cerebrospinal fluid (CSF). Communication via the fourth ventricle with the subarachnoid space, allows for the flow of CSF from the ventricular system to provide a protective cushioning of CSF around the brain (Crossman and Neary, 2005). The complex regulation of CSF flow within the brain can become compromised due to the presence of mass lesions, including tumours (Fukuda et al., 2014).

Within the posterior fossa, tumours and the associated oedema, can obstruct the fourth ventricle (Schmid and Seiler, 1986), resulting in hydrocephalus due to obstruction of the CSF pathways or its absorption (Rangel-Castilla et al., 2008). As a result, uncompensated increases in intra-cranial volume can result in elevated intra-cranial pressure (ICP), with the potential risk of brain herniation (El Ahmadieh et al., 2013). Hydrocephalus has been defined as “an active distension of the ventricular system of the brain resulting from inadequate passage of CSF from its point of production within the cerebral ventricles, to its point of absorption into the systemic circulation" (Rekate, 2008). Hydrocephalus resulting from the presence of a tumour or alternative mass lesion is referred to as obstructive hydrocephalus. Management of this form of hydrocephalus requires treatment of the underlying mass lesion, with the potential of supplementary CSF surgical management techniques such as shunting, being required (Rangel-Castilla et al., 2008).

2.6 Anatomy of the Brainstem

The brainstem is composed of the medulla oblongata, pons and midbrain. It is directly connected to the cerebellum, is continuous caudally with the spinal cord and rostorally the midbrain is continuous with the diencephalon of the forebrain (Crossman and Neary, 2005). Ascending and descending pathways involved in the transmission of sensory and motor signals within the CNS are located within the brainstem (Shumway-Cook and Woollacott, 2007). One of the main descending pathways is the motor pathway, composed of the

corticospinal and corticobulbar tracts which control voluntary skeletal muscle activity of the body and face. The somato-sensory afferent pathways of the brainstem conduct sensations of pain, temperature, proprioception and touch and are continual with the spinal cord in the medulla (Angeles Fernandez-Gil et al., 2010). Cranial nerve nuclei three to twelve are located within the brainstem and are involved in significant body functions including sleep, arousal, sensation and swallowing (Crossman and Neary, 2005).

2.7 Pathophysiology of Posterior Fossa Tumours

Several subtypes of brain tumour can occur within the posterior fossa but similarly to cortical brain tumours, all rely heavily on the involvement of blood vessels for survival and growth. Blood supply to the tumour can be provided by the pre-existing vasculature of the invaded cerebral tissue and also by the process of angiogenesis (Vaupel et al., 1989). Angiogenesis is the process of new vessel development and tumour growth is believed to be dependent on this process (Wu, 1996). Normal brain vasculature is highly specialised and the blood brain barrier (BBB) restricts movement between the intracerebral and extracerebral circulatory systems (Jain et al., 2007). Pathology, secondary to the presence of a brain tumour, leads to increased vascular permeability of the BBB, causing both structural and functional compromise of the BBB (Jain et al., 2007). Vascular endothelial growth factor A (VEGFA), a platelet derived growth factor, is highly expressed by tumour cells and contributes to the compromise of the BBB by inducing permeability and angiogenesis. This permeability of the BBB can result in the formation of vasogenic oedema, due to altered restriction on movement across the barrier. This process is frequently observed in brain tumours. Formation of vasogenic oedema is strongly associated with high grade, aggressive tumours but also occurs in more benign histologies, such as meningiomas (Papadopoulos et al., 2004).

2.8 Posterior Fossa Tumours

2.8.1 Metastases

In the adult population, brain metastases are the most frequently occurring intracranial tumour as well as the most frequently occurring posterior fossa tumour. Autopsy studies have identified, 20-40% of individuals who develop metastatic disease will have a lesion metastasise to the brain (Weil et al., 2005). Within the brain, 80% of the metastatic lesions

occur within the cerebral hemispheres, 15% in the cerebellum and 5% within the brainstem (Buckner et al., 2007). The most frequently diagnosed primary tumour sites that metastasise to the brain are lung and breast cancer (Lassman and DeAngelis, 2003).

Irish data published in the National Cancer Control Programme (NCCP) Annual Report 2012, highlighted 77 adult cases of brain metastases requiring surgical intervention across the two neurosurgical centres in the Republic of Ireland - Beaumont Hospital and Cork University Hospital, in 2012. This equates to 13% of the gross number of surgical interventions for brain tumour conducted in Ireland in 2012. The report outlined 25 of the cases had a primary originating in the lung (25/77; 32%) and 16 primaries originating in the breast (16/77; 21%), mirroring international trends.

2.8.2 Haemangioblastoma

CNS haemangioblastomas, are benign vascular tumours occurring most frequently in adults, accounting for 2% of intracranial tumours and 7% - 10% of posterior fossa tumours (Wan et al., 2011). This tumour type may have of solid or cystic structure, which plays a role in determining the activity of the tumour (Tomasello and La Torre, 2014). Haemangioblastomas can occur as a solitary lesion, however approximately 20%-30% of tumour occurrences are associated with Von Hippel-Lindau (VHL) syndrome (Neumann et al., 1989). VHL disease is a familial syndrome, associated with the presence of vascular lesions in various organs, including haemangioblastomas of the retina and CNS, renal cell carcinomas and cysts, pancreatic tumours and cysts, endolymphatic sac tumours and phaeochromocytomas (Richard et al., 2004). VHL disease is believed to account for approximately one third of patients with a CNS haemangioblastoma (Maher et al., 2011).

In 2012, the NCCP annual report highlighted ten adult cases of intra-cerebral haemangioblastoma requiring surgical intervention in 2012. This indicates 1.5% of the total number of brain surgeries in the Irish republic in 2012, being due to the presence of a haemangioblastoma.

2.8.3 Meningiomas

Meningiomas are benign neoplastic lesions which account for approximately 20% of all intracranial tumours (Velho et al., 2012), with approximately 9-10% developing in the posterior cranial fossa (Roberti et al., 2001). Within the posterior fossa there are several

locations associated with meningioma occurrence including cerebellar convexity, tentorial, cerebellopontine angle, jugular foramen, petroclival, peritorcula, and foramen magnum (Jung et al., 2014). This tumour type arises from the arachnoid granulations and is closely related to the venous sinuses, with the tendency to compress brain tissue rather than invade it (Lindsay and Bone, 2004).

The 2012 NCCP Annual Report summarised 86 surgical interventions conducted between Beaumont Hospital and Cork University Hospital, were due to the presence of a cerebral meningioma. This equates to 14% of all cerebral surgical interventions in 2012, in the Republic of Ireland.

2.8.4 Paediatric posterior fossa tumours

Significant variations exist in the tumour profile of lesions occurring in the posterior fossae of children when compared with that of adults. Medullablastoma is a commonly occurring paediatric brain tumour that arises from cerebellar tissue and accounts for approximately 25% of all childhood brain tumours (Kumar et al., 2015). They are classified as primitive neuroectodermal tumours (PNET) and account for only 1% of all adult CNS tumours (Brandes and Franceschi, 2014). In paediatric cases, the tumour most commonly occurs in the vermis of the cerebellum but tends to originate in the cerebellar hemispheres of adults. Variations also exist in the mean survival rates between age groups, with the 15 year mean survival rate in children being 53% and in adults 43% (Smoll, 2012). Astrocytomas arising within the posterior fossa also occur more frequently in paediatric cases, with an associated expected benign course following surgical resection and a 10-year survival rate of more than 95% (Burkhard et al., 2003). In an Irish series consisting of 79 paediatric posterior fossa tumour patients, 41% of the population were diagnosed with pilocytic astrocytomas and 32% with PNET (O'Brien et al., 2001). In an international review of the incidence and survival of individuals diagnosed with an astrocytoma over a fourteen year period, the age profile identified 38% of the study population were paediatric cases, 22% adolescents and 40% adults (Burkhard et al., 2003). The cerebellum was the most frequent site of growth in children (67%), with adults displaying no significant variations between supra and infra-tentorial location for the occurrence of astrocytomas.

2.9 Management techniques of posterior fossa tumours

Management of lesions in the posterior fossa requires timely intervention due to the compact nature of this area of the brain and the associated risk of brainstem compression (Bullock et al., 2006). Raised intracranial pressure (ICP) can be of primary or secondary origin. Tumours, traumatic bleeds, non-traumatic haemorrhage and hydrocephalus are classified as primary causes of raised ICP with hypoxia, hypertension and seizures classified as secondary causes (Rangel-Castilla et al., 2008). In a cohort of posterior fossa trauma patients, reduction of intracranial pressure and the potentially associated mass effect on the fourth ventricle was identified as the primary goal of management (Nixon et al., 2014).

2.9.1 Steroids

Clinical use of steroids in individuals with primary or secondary tumours of the central nervous system is well documented, for their role in management of peri-tumoral oedema. Research has shown that between 70–100% of patients with intrinsic brain tumours will have steroids as an independent modality or in conjunction with cytotoxic therapy during the course of their treatment (Hempen et al., 2002). Brain oedema is believed to be caused by an expansion of brain volume due to an increase in water and sodium content (Kaal and Vecht, 2004). Vasogenic oedema is the most commonly occurring type of cerebral oedema in this population and results due to disruption of the BBB which allows fluids to leak from the blood into the brain parenchyma (Dubois et al., 2014). Research has shown oedema to accumulate around brain tumours at a rate of 14 to 78 ml/day (Kaal and Vecht, 2004). The role of corticosteroids has been shown to influence this alteration in permeability by influencing the rate of permeability across the membrane, with noted radiological changes in oedema levels (Andersen et al., 1994).

Dexamethasone is the most commonly employed corticosteroid agent in the management of tumour related cerebral oedema (Ryan et al., 2012). It is approximately six times more potent than prednisone and takes full effect within the body between 24 to 72 hours (Ryan et al., 2012). It functions by blocking inflammatory pathways, by acting on glucocorticoid receptors which reduce vessel permeability of tumour capillaries and increase extracellular fluid clearance (Fan et al., 2014). While it is the steroid of choice in the management of this population, it is associated with both positive and negative side effects. In a retrospective review of dexamethasone dosages and side effects associated with its administration,

Hempen (Hempen et al., 2002) investigated its role in the management of neurological consequences of primary and secondary brain tumours and its role in the management of associated treatment sequelae. Dexamethasone was found to effectively reduce the associated neurological side effects of primary and secondary brain tumours and the symptoms of radiation therapy. Dexamethasone also plays an essential role in the reduction of mass effect, associated with peri-tumoral oedema (Roth et al., 2010). As previously outlined, the anatomy of the posterior fossa restricts volume increases with the associated risk of compression on the cerebellum and brainstem, with increasing oedema. Mass effect in this area of the brain could result in herniation through the foramen magnum with associated death (Gurol and St Louis., 2008). Thus the role of steroids in individuals with a posterior fossa tumour could have a life-saving role. Negative consequences associated with steroid use includes steroid induced diabetes (Roth et al., 2010), myopathy (Owczarek et al., 2005) and psychiatric consequences (Ross and Cetas, 2012). While the increased risk of fracture in the general medical population is believed to be between 50 – 100% with oral corticosteroid use, the associated impact with dexamethasone administration in brain tumour patients has not been established (Ryan et al., 2012).

2.9.2 Radiotherapy

Radiation therapy is a treatment approach utilised in the management of individuals with high grade tumours. Radiation energy works by producing ions in the cells of the tissue which it passes through and subsequently disrupts the molecular structure of the cells. The formation of free radicals leads to the breakdown of tissue, including tumour cells (Kirthi Koushik et al., 2013). Radiation therapy can be used as an independent treatment modality or in conjunction with surgery and/or chemotherapy, referred to as adjuvant therapy. Optimal timing for the commencement of treatment is believed to be two to three weeks post-operatively, to allow fibroblastic proliferation and healing of the surgical wound. A delay of greater than eight weeks in commencement of radiation can significantly reduce its effectiveness due to the tumour cells ability to repopulate within this timeframe (Kirthi Koushik et al., 2013).

Radiation therapy often employed in the management of brain tumours, has been shown to cause several side effects including headache, drowsiness, fever, vomiting and worsening neurological side effects (Soussain et al., 2009). While these symptoms may occur acutely

during delivery of the radiation therapy, delayed deficits associated with the development of radiation necrosis can also be observed. Risk of development of radiation induced necrosis is highest in the first two years but the threat of development of this complication can persist for several years, even decades (Ruben et al., 2006). Radiation necrosis has the ability to produce similar side effects and deficits to that of tumour tissue and poses difficulty for surgeons in differentiating the tissue type, as these tissues can appear similar on MRI scan and in clinical presentation. Irradiated patients have also been shown to have a seven fold increased risk of developing a secondary tumour within the margins of the radiation treatment zone. Meningiomas are the most frequently occurring post radiation tumour, accounting for 70% of radiation induced tumours (Kleinschmidt-Demasters et al., 2006).

2.9.3 Chemotherapy

The role of chemotherapy in the treatment of brain tumours is limited to chemotherapeutic agents that have the ability to infiltrate the BBB. As previously discussed, higher grade brain tumours result in the destruction of cells involved in the maintenance of the integrity of the BBB, highlighting the role of chemotherapy in the management of high grade brain tumours. Chemotherapy can be administered as an independent treatment modality, however it is routinely administered post-surgical excision or in conjunction with radiotherapy as a concomitant treatment approach (Salmaggi et al., 2011). Temozolomide, a second-generation alkylating oral chemotherapeutic agent, has demonstrated the ability to cross the BBB and achieve CSF concentrations of approximately 30% of plasma concentrations in animal and human models (Ebert et al., 2003). In a pioneering study that investigated the combined treatment approach of radiotherapy and Temozolomide, in newly diagnosed Glioblastoma Multiforme (GBM) patients, a median increase in survival of 2.5 months or a relative reduction in the risk of death of 37 %, was identified (Stupp et al., 2005). This regimen, The Stupp Protocol, is now an internationally administered treatment approach in the management of high grade gliomas.

While the role of chemotherapy in high grade primary brain tumours such as GBM has been established, its role in the management of posterior fossa tumours may be limited, as GBM tumours have been shown to be much less likely to occur in the posterior fossa when compared with the cerebrum (Chakrabarti et al., 2005).

2.9.4 Surgery

The most effective treatment option in the management of elevated ICP is the surgical removal of the underlying space occupying lesion (El Ahmadieh et al., 2013). Two frequently utilised surgical procedures to expose and access a posterior fossa lesion include a craniectomy (complete removal of the bone) or craniotomy (bone flap fixation) (Legnani et al., 2013). Historically, craniectomy was the most frequently utilised surgical technique giving excellent exposure, however, it resulted in the cerebellum and dura being protected by muscle and scalp alone (Bucy, 1966). Craniotomy, due to the replacement of the bone-flap post surgery, has been shown to provide increased protection of the posterior fossa, with a reduced complication rate (Gnanalingham et al., 2002). Legnani et al (2013) retrospectively analysed 152 consecutive patients admitted to a neurosurgical centre, over a three year period, who underwent a craniotomy or craniectomy procedure, due to the presence of a posterior fossa tumour. One hundred patients underwent a craniotomy (66%), while 52 patients underwent a craniectomy (34%). Results of post-operative complication rates, related to the surgical technique, was 7% for the craniotomy group and 32.6 % for the craniectomy group (<0.0001), indicating a statistically significant reduced rate of surgical complication, related to craniotomy when compared with craniectomy. The post-operative complications identified in the whole sample included pseudomeningocele (an abnormal collection of CSF), CSF leak, wound infection and hydrocephalus. The integrity of the dura mater was identified as a key component in determining the success of the surgery, as 50% of the patients who did not have a complete dural closure post-operatively, developed issues with CSF flow and development of fluid collections. Other researchers have identified similar surgical complications in those undergoing surgery of the posterior fossa (Dubey et al., 2009) with CSF leaks, meningitis, wound infection, hydrocephalus and cerebellar haematoma being identified as the associated risks.

While several surgical complications can be associated with a neurosurgical intervention to this aspect of the brain, even successful surgery carries significant risk. The characteristics of the tumour, exact location of the surgery and skill of the surgeon, all influence the outcome of the patient. The compact nature of the posterior fossa and the complexity of the cerebellum in the control and regulation of movement, places risk on the patient in relation

to the execution and modulation of skilled movements as demonstrated in gait and upper limb activities.

2.10 Clinical Presentation

Clinical deficits associated with the presence of a brain tumour are resultant from the focal disruption of the lesion itself, associated increase in intra-cranial pressure and surgical techniques employed in managing the tumour. This is particularly relevant in the posterior fossa, due to the limited capacity for tissue adaption due to restricted space and the rigidity of the cranium. The presence of the cerebellum, brainstem and fourth ventricle within the posterior fossa, give rise to associated dysfunction when compromised. Ataxia is a very common feature observed in individuals with dysfunction of the posterior fossa. Involvement of the cerebellum or its input and output pathways, can result in ataxia of voluntary limb movement or gait, which can lead to high amplitude tremors associated with ataxic movement (Bastian, 1997). Cerebellar gait ataxia has typical features including increased step width, variability of foot placement, irregular foot trajectories resulting in a stumbling walking path with very high movement variability and, an associated increased falls risk (Ilg and Timmann, 2013). Postural instability with associated antero-posterior (AP) sway, postural tremor and increased intersegmental movements of the head, trunk and legs, contributes to the characteristic patterns identifiable in this population of patients (Morton and Bastian, 2007). Increased reaction time and an associated reduced speed in execution of tasks, is also characteristic of this population. Deficits of multi-joint movements, called dyssynergia, manifests in movements with associated prolonged duration, decreased maximal velocity and an increase in spatial variability, resulting in variability between trials (Marsden and Harris, 2011). Emerging evidence has also highlighted the role of the cerebellum in working memory, implicit and explicit learning and language, indicating the potential for higher level deficits with the capacity to influence rehabilitation and new skill acquisition (Desmond and Fiez, 1998). In conjunction with the cerebellum, the brainstem also has the capacity to impact on motor control due to its role as a junction for several of the main ascending and descending pathways of the brain (Angeles Fernandez-Gil et al., 2010).

While the anatomical structures of the posterior fossa are heavily involved in movement and control of movement sequencing within the body, minor shifts in volume within this

area, can result in mortality due to altered CSF flow, compression of eloquent tissues and distortion of brainstem structures. In the clinical and rehabilitation setting, the patient with a posterior fossa tumour may never be well enough to engage in treatment for their movement deficits, due to the risk of mortality associated with tumours of this region of the brain (Jung et al., 2014).

2.11 Conclusion

This chapter of the thesis has reviewed the global and national data on cancer and brain tumours, outlined anatomy of the posterior fossa and its cerebral components and reviewed medical and surgical management techniques utilised in the treatment of this tumour type. In chapter three of the thesis, rehabilitation in cancer, with particular emphasis on rehabilitation of patients with deficits secondary to posterior fossa lesions, will be explored.

Chapter 3: Rehabilitation in the Management of Brain Tumour Patients

3.1 Introduction

Chapter three of this thesis aims to provide a comprehensive overview of the role of rehabilitation in the management of cancer patients, with particular focus on the role of rehabilitation in those with brain tumours. This chapter also provides a detailed outline of a systematic review that was completed over a two year period, as part of the Master's programme, systematically reviewing the entire catalogue of available literature on rehabilitation practices in the management of individuals with tumours of the posterior fossa.

3.2 Brain Tumours

Tumours of the cerebrum are complex and diverse pathological anomalies that include primary neoplasms, that arise from normal cellular constituents and embryologically displaced tissues and brain metastases, which derive from a distantly located malignant cancer site (Giordana and Clara, 2006). Given the increasing incidence of brain tumours (BT), the complexity of their management , the chronic and progressive nature of symptoms and an ageing population, increasing attention needs to be focussed on this patient cohort to optimise management (Gamble et al., 2011). Historically, diagnosis of a brain tumour was generally associated with a terminal outcome, however, continuing advances in cancer therapies and increased survival, has resulted in cancer management adopting a profile of chronic disease (von Eschenbach, 2004). Brain tumour patients are now living longer with deficits associated with the tumour and the cancer treatments employed in its management (Loescher et al., 1989).

In a review of surgical approaches in the management of a single brain metastases, complication rates associated with an "en bloc" versus "piecemeal" excision approach was investigated (Patel et al., 2015). A higher rate of associated side-effects was noted in the "piecemeal" excision approach (19%), however, both surgical approaches resulted in a variety of side-effects including neurological deficits, deep vein thrombosis, infections and haemorrhages. Radiation therapy, often employed in the management of brain tumours, has been shown to cause several side effects including headache, drowsiness, fever, vomiting and worsening neurological side effects (Soussain et al., 2009). Given the

symptoms associated with a brain tumour and the potential for development of treatment associated side-effects, a shift towards comprehensive rehabilitation practices to manage this population has occurred over the previous 40 years.

3.3 Introduction to Rehabilitation

Rehabilitation has been defined as "a problem-solving educational process aimed at reducing disability and handicap experienced by someone as a result of disease or injury" (Wade, 1992). The role of rehabilitation as a vital component of treatment, to assist functional recovery within certain neurological populations is well established (Taylor et al., 2014, Rose, 1999). In neuro-oncology patients, the neurological deficits combined with uncertainty and fear of a cancer diagnosis, creates a more challenging presentation to manage.

3.4 Cancer Rehabilitation

Cancer rehabilitation is considered to be a relatively new sub-speciality within the rehabilitation field, which should be incorporated into routine care of all cancer patients (Ganz, 1990). The earliest research available that explored rehabilitating cancer patients was undertaken by rehabilitation specialists, who hypothesised that the application of pre-existing rehabilitation principles to cancer sufferers should provide similar benefits as non-cancer patients, with similar deficits (Dietz, 1969, Rusk, 1964). Considered the forefathers of oncology rehabilitation, their pioneering research encouraged subsequent researchers to explore the potential positive impact rehabilitation could have on the outcomes of this population of patients. An early definition of cancer rehabilitation put forward by Dietz (1981), introduced this rehabilitation concept under four subheadings including; preventative, restorative, supportive and palliative. These four subheadings aimed to provide the appropriate level of rehabilitation input required by patients at the varying stages of the disease process. The terminology defining cancer rehabilitation has continued to evolve since Dietz original work. Dudas (1984) defined cancer rehabilitation as "a dynamic process directed toward the goal of enabling persons to function at maximum levels, in all life spheres, within the limits imposed by the disease", while Mayer and Connor (1989) recognised the importance of rehabilitating "individuals within their environments", to maximise rehabilitation gains. Modern definitions have aimed to adopt a rehabilitation

philosophy that is holistic in approach and incorporates the diverse skill and knowledge of the multidisciplinary team (Cheville, 2005).

Comparable improvements in rehabilitation outcomes have been noted between varying oncology populations. In a retrospective review of 159 inpatients in a rehabilitation facility, comparable functional gains were made across diverse oncology populations, including diagnosis of primary brain tumour, breast cancer, spinal tumour and a category called "other", which incorporated any other cancer patient who met the desired inclusion criteria and had to be grouped into a subgroup, for analysis (Marciniak et al., 1996). This study also revealed that the presence of metastatic disease or concurrent radiation therapy, during the course of rehabilitation, did not negatively impact on the degree of functional improvement. Another study (Cole et al., 2000) looked at the functional gains across nine cancer subgroups and found results comparable with that of Marciniak et al (1996). These results highlight the potential for all cancer patients, with cancer associated deficits, to benefit from a period of rehabilitation, regardless of tumour location or subtype, including brain tumours of primary or secondary origin.

3.5 Brain Tumour Rehabilitation

Although increasing advances in the management of brain tumour patients are occurring every year, a survey conducted in the United States revealed that 50% of rehabilitation hospitals treat a maximum of ten brain tumour patients per year (Boake and Meyers, 1993). Throughout the literature, comparisons have been drawn between rehabilitation of brain tumour patients and other neurological conditions. Researchers have shown that brain tumour patients possess the potential for comparable functional gains and outcomes (Tay et al., 2009). Within this population, coping with the psychological impact, reduced income and socioeconomic implications, increased demand for health care, social and vocational services, and caregiver burden (Tang et al., 2008), as well as considering decisions regarding cancer therapies, all place extra stresses on the BT patient (Cheville, 2001). Cognitive impairment has been highlighted as one of the most frequently occurring deficits in this population, with limb weakness, the second most frequently occurring consequences of a brain tumour (Marciniak et al., 1996, Mukand et al., 2001). O Dell et al (1998) retrospectively reviewed all brain tumour patients admitted to a rehabilitation centre over a 30 month time period. Forty patients, with varying tumour type, were included and

matched with Traumatic Brain Injury (TBI) patients of similar age, Functional Independence Measure score (FIM) and gender. The researchers found that within the brain tumour group, more favourable outcome was directly linked to diagnosis of a meningioma or a left sided lesion, without receiving concomitant radiation therapy. When compared to TBI patients, FIM scores were statistically significant for two of the subsections of the form but these benefits were not significant when variances in length of stay were adjusted for. The literature has shown that with similar deficits, brain tumour participants tend to be discharged home quicker than TBI participants. This is believed to be linked to the potential terminal diagnosis that these patients may have, which encourages optimally facilitated discharges. In a similar study (Huang et al., 2000), a group of brain tumour patients and TBI patients were matched on the basis of age and side of lesion. This study revealed similar results in FIM scores, at admission and discharge and overall function was comparable between the groups. This study also demonstrated a reduced length of stay in the brain tumour population. Comparison of outcome with stroke has also been investigated (Huang et al., 1998). This study found similar levels of improvement between the two groups on the overall FIM score and when subdivided into certain components including the mobility, Activities of Daily Living (ADLs) and cognition elements of the measure. A significant difference was noted on comparison of the length of stay, both in the acute setting and in rehabilitation environments. This finding is similar to that already noted in the comparisons between TBI and BT outcomes. Similar treatment approaches in the management of TBI and BT patients have shown maintained benefits in BT patients for an average of eight months (Sherer et al., 1997). Focus on the physical consequences of brain tumours remains of paramount importance to the recovery of this population, however, associated concerns and anxieties (relationship, employment, tumour recurrence) cannot be underemphasized (Ownsworth et al., 2009).

3.6 Multidisciplinary (MDT) role in neuro-oncology rehabilitation

The complexity of rehabilitation needs in neuro-oncology patients has highlighted the importance of collaborative and cohesive multi-disciplinary approaches to management. The World Health Organisation (WHO) defines MDT rehab as “coordinated delivery of multidimensional rehabilitation intervention provided by two or more disciplines, in conjunction with medical professionals, which aims to improve patient symptoms, and

maximise functional independence and participation (social integration) using a holistic biopsychosocial model of care, as defined by the International Classification of Functioning, Disability and Health (ICF)" (Stucki et al., 2003). A lack of research is available investigating the role of the MDT in brain tumour management when compared with alternative neurological populations (Khan et al., 2007, Turner-Stokes et al., 2005, Stucki et al., 2003, Monaghan et al., 2005). As previously outlined, this population of patients demonstrate a complex range of bio-psychosocial difficulties that would benefit from an MDT approach to management and care. While the importance of the role of the medical and surgical MDT has long been established in brain tumour care pathways (Landonio, 2005), the role of allied health care professionals in management of this population has had limited investigation. In a recent Cochrane Review of the literature, Khan et al (2013) investigated multidisciplinary rehabilitation practices post treatment, for a primary brain tumour. No randomised or case controlled trials were identified by a systematic review of the literature and this Cochrane collaboration is based on the results of twelve observational studies. The quality of the available evidence limited the conclusions that could be extrapolated but the authors concluded that the poor quality of available evidence does not distract from the need for multidisciplinary involvement but further high quality research is required to identify the merits of this intervention. Although the quality of included evidence was poor the investment of resources in conducting a Cochrane review on this topic, highlights the increasing awareness and need of quality evidence in this field.

3.7 Rehabilitation of posterior fossa tumour patients

The role of rehabilitation in the management of cancer patients has been clearly demonstrated to date. Research has highlighted the benefits to be gained from rehabilitation regardless of the location of the cancer or the WHO grade (Louis et al., 2007). The WHO classification system is the internationally accepted system of brain tumour classification, based on the tumour's histological components. Unfortunately, extreme care must be considered when dealing with tumours of the central nervous system due to the complex and delicate nature of the involved brain tissue. Several factors including the space occupying lesion (Nakaya et al., 2010), associated vasogenic oedema (Gurol and St Louis, 2008), surgical compromise (Jahangiri et al., 2012) and hydrocephalus (Goel, 2002) can compromise the tissues of the brain and spinal cord. The posterior cranial fossa is an area of

the skull that is located between the foramen magnum and tentorium cerebelli and houses the highly complex cerebellum, brainstem and fourth ventricle (Levin, 2002). The rigid nature of the cranium means the presence or expansion of a mass in this area of the brain can potentially cause compromise to the brainstem and cerebellum with the possibility of fourth ventricle blockage causing hydrocephalus (Levin, 2002). Dysfunction of the cerebellum can result in reduced co-ordination, manual dexterity compromise as well as gait and balance dysfunction. An ataxic gait pattern is often characteristic of cerebellar compromise and features include reduced gait speed and cadence (Palliyath et al., 1998), increased step width (Ilg et al., 2007) and abnormal inter-joint coordination (Morton and Bastian, 2003). A close interaction has been revealed between altered balance and ataxia in individuals with cerebellar compromise (Marquer et al., 2014). The brainstem contains several nuclei involved in essential processes including the vestibular, red and reticular nuclei, which play a role in postural control, locomotion, arousal and awareness (Shumway-Cook and Woollacott, 2007). The floor of the fourth ventricle is formed by the brainstem and its lateral wall and roof formed by the cerebellum, indicating dysfunction to one of these structures can cause a negative impact on all (Su and Young, 2011).

As previously identified, there has been increasing attention towards the rehabilitation of brain tumour sufferers, however there is a significant dearth in the volume of research that has specifically investigated the rehabilitation of individuals with a tumour occurring in the posterior fossa. Nine studies were included in a systematic review that reviewed rehabilitation in the management of individuals with cerebellar dysfunction (Martin et al., 2009). This review included a cohort with varying primary diagnosis, including Multiple Sclerosis (MS), Traumatic Brain Injury (TBI), BTs and hereditary ataxia. To treat the commonly occurring deficits noted in individuals with cerebellar compromise, balance and gait training (Marsden and Harris, 2011), Frenkel's exercise (Armutlu et al., 2001), vestibular habituation exercises (Brown et al., 2006) and proprioceptive neuromuscular facilitation (Perlmutter and Gregory, 2003) were identified as the commonly adopted rehabilitation approaches utilised. Reproduction of the programmes would remain difficult due to poorly documented specifics of exercise prescription and progression.

Despite the availability of research investigating rehabilitation of the symptoms associated with involvement of the posterior fossa, a review has not previously been undertaken that

has investigated the role of rehabilitation in individuals with the sole diagnosis of a tumour of the posterior fossa.

3.8 Systematic Review

3.8.1 Introduction

A systematic review was undertaken with the aim of investigating the rehabilitation techniques employed by rehabilitation therapists (Physiotherapist or Occupational Therapist), in the management of impairments, activity limitations or deficits in participation, in individuals with tumours of the posterior fossa. The following section details the methodology, analysis and results of the systematic review. The findings of the systematic review are also discussed in relation to the current and future status of rehabilitation, in this population of patients.

3.8.2 Methodology

To ensure this systematic review was conducted in a comprehensive and systematic fashion, the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) standardised reporting guidelines were followed to conduct and report the findings (Stroup et al., 2000). In June 2013, a comprehensive search of the literature was conducted and included the search engines Pubmed, The Cochrane Library, Embase, Ebsco Host and Sciverse. A comprehensive search string was established that included the search terms, “cerebellar neoplasm”, “posterior fossa tumour”, “brainstem neoplasm”, “infra-tentorial neoplasm”, “tumour”, “balance”, “gait”, “physical therapy” and “neurologic gait disorders”. A copy of the full search string is included as appendix one and two. The reference lists for all the identified articles were searched for any further potential articles for inclusion. The search did not restrict article inclusion based on year of publication or non-English language publication. To ensure the systematic review remained current, the original search-string was reanalysed in April 2015, adhering to the same search criteria, to ensure any newly available research on the topic of rehabilitation in posterior fossa patients, was identified and included in this systematic review. No new appropriate studies were identified on the supplementary searching, for inclusion in the review.

A set of inclusion criteria was established to identify relevant and eligible articles for inclusion. The inclusion criteria included: (1) All study designs (2) The study population was

that of an adult or paediatric population who had undergone a surgical intervention, due to the presence of a tumour in the cerebellum, brainstem or fourth ventricle (posterior fossa). Inclusion of paediatric participants in the systematic review is in contrast with the age related inclusion criteria of the prospective study. Inclusion of paediatric studies in the systematic review ensured all potential rehabilitation and treatment approaches pertaining to the posterior fossa were included in the review, ensuring a comprehensive and complete review of rehabilitation for the posterior fossa. (3) Studies that had utilised a rehabilitation programme conducted by a physiotherapist or occupational therapist, for the treatment of balance, gait, upper limb dexterity or dizziness deficits. Outcomes of interest were those at the level of impairment, activity limitation or participation restriction. (4) Posterior fossa tumours that did not originally originate in the internal auditory meatus. This is a common site of origin of vestibular schwannomas and their management and clinical course differs significantly, to tumours originating within the posterior fossa itself. Previous literature has classified posterior fossa tumours in a similar fashion (Karakaya et al., 2000).

On identification of potentially suitable articles for inclusion, the researcher read the titles and/or abstracts of the identified references to determine those which met the inclusion criteria. All references of studies deemed irrelevant were eliminated. Studies that were considered to be relevant, based on this process, were read in duplicate by two independent reviewers (KM and RG). Any disagreement that was encountered was managed by consensus. A process of data extraction was undertaken, that gathered information from the appropriate studies including study type and setting, patient demographics including age and sex, clinical characteristics including tumour location, timeframe since surgery, rehabilitation interventions based on the FITT (frequency, intensity, time and type) principles, outcome measures utilised in the studies, number of interventions and follow-up period.

On completion of a systematic search of the literature, the only identified studies that complied with the inclusion criteria were case series, and as a result was the only study type included in this systematic review. To ensure best epidemiological practice, the CARE (case reports) checklist was used to critically appraise the selected articles for inclusion in the systematic review (Gagnier et al., 2013). A copy of this checklist, used to evaluate the quality of each study in the systematic review is available as appendix three to seven inclusive. Two

investigators (KM and RG) independently assessed and appraised the methodological quality of each included study. During the process two areas of disagreement occurred, when conducting the literature appraisal. The identified discrepancies occurred in relation to one article (Ada et al., 2009). The identified discrepancies pertained to the inclusion of relevant milestones within the article and reference to prognostic characteristics, where applicable within the article. These discrepancies were resolved by discussion.

The study design of each of the included studies in this systematic review was case studies. Due to the clinical and methodological heterogeneity of the five included studies, a narrative review of the results is presented, due to an inability to conduct a meta-analysis. To ensure optimum standards in the conducting and presentation of the review, the Cochrane Handbook guidelines were followed (Higgins and Green, 2011). The narrative review of the results includes the number of participants within each study, duration of intervention, rehabilitation techniques utilised in the treatment of the participants, outcome measures used and follow-up timeframe. An assessment of the methodological quality of each study has been reported within the review, as well as a discussion of the limitations.

3.8.3 Results

A Prisma flow diagram is included as appendix eight, to give an accurate graphical presentation of the search strategy conducted in the identification of appropriate studies, for inclusion in the systematic review. The flow diagram of updated results obtained with the updated search in April 2015 is available as appendix nine. No supplementary, appropriate articles were identified on the updated search, for inclusion in the systematic review.

The search yielded 3,482 articles from five databases including Pubmed, The Cochrane Library, Embase, Ebsco Host and Sciverse. An additional five articles were identified for potential inclusion by hand searching reference lists. With removal of duplicates 3,276 articles were available for consideration for inclusion. The titles or abstract was reviewed of the 3,276 articles to determine suitability and as a result 3,254 articles were subsequently excluded. The full text of the remaining 22 articles was read and as a result only five full text articles achieved the desired inclusion criteria and as a result were included in the

systematic review. Reasons for exclusion were tumours not specifically located in the posterior fossa and participants not receiving a period of rehabilitation.

3.8.3.1 Study Characteristics

A table depicting the characteristics of the five included studies is available as appendix ten. The study locations varied across the studies. Two studies were conducted in the United States (Gill-Body et al., 1997, Cremer, 1998), one in Australia (Ada et al., 2009), one in Canada (Betker et al., 2006) and one in Turkey (Karakaya et al., 2000). The size of the patient cohort ranged from a single participant (Ada et al., 2009) to 20 participants (Karakaya et al., 2000), diagnosed with a tumour of the posterior fossa. The age profile of the study subjects also varied across the studies. A total of 52 participants were included in the studies but of these individuals only 24 met the inclusion criteria of being diagnosed with a tumour of the posterior fossa. Participants that did not meet inclusion criteria had varying diagnosis including cerebellopontine angle tumour (Karakaya et al., 2000), cerebrotendinous xanthomatosis (Gill-Body et al., 1997), stroke (Betker et al., 2006) and TBI (Betker et al., 2006). Of the included studies, all lacked the inclusion of a comparison group.

3.8.3.2 Study Quality

The overall quality of the included studies, within the systematic review was poor. As only case studies were identified as satisfying the inclusion criteria, an immediate low level of epidemiological quality was assumed. In terms of the internal validity of the studies, infrequent reporting methods were used to obtain informed consent and a lack of consistency in the reporting of adverse outcomes and diagnostic challenges were evident in the majority of studies. A period of follow-up was documented as occurring in only one of the studies (Ada et al., 2009). A follow-up timeframe of two weeks was used in the study but this short observation period, while superior to no follow-up, prevented robust conclusions about the long term effectiveness of the rehabilitation techniques utilised in the management of deficits, as a result of a tumour of the posterior fossa.

3.8.3.3 Rehabilitation Techniques

Within the five included studies in the systematic review, all rehabilitation programmes were delivered by a physiotherapist/physical therapist. While the inclusion criteria considered rehabilitation programmes delivered by either the discipline of physiotherapy or

occupational therapy, no studies were identified in which a programme of occupational therapy was delivered to this cohort of patients, to treat the deficits associated with posterior fossa tumours.

Within the included studies the rehabilitation programmes and the associated interventions were aimed at treating a range of impairments and activity limitations. A large degree of variation existed with regards to the rehabilitation programmes and variances in frequency, intensity, type and time-frames were common throughout the five studies.

Ada et al (2009) investigated the ability to train upper limb dexterity in a five year old child, who had undergone a neurosurgical procedure for the excision of a large midline cerebellar tumour, three and an half years prior to being recruited for the study. At time of enrolment in the study, the participant had no upper limb weakness but experienced residual bilateral upper limb ataxia, the right being more severely affected. As a result the right upper limb was chosen as the limb of choice for involvement and investigation in the study. The treatment technique was a computer based programme using an electro-goniometer attached to the participants forearm to monitor elbow flexion and extension as she tracked movements of a pseudo-random target on the computer. The targets moved irregularly on the screen and at varying frequencies giving an element of unpredictability to the task. Twelve sessions of this treatment were provided in the participant's home by a parent, who was also a physiotherapist. A maximum of ten, thirty second trials were completed during each treatment session, using varying frequencies. To optimise compliance of the participant, a standardised number of sweets were used as reinforcers, to encourage engagement with the programme, when she was not eager to engage. All sessions were conducted in the participant's home in the late afternoon.

Betker et al (2006) also used technology to deliver a rehabilitation programme focusing on the use of video games in the balance training of three participants. Each of the participants had a varying primary diagnosis including a twenty year old post cerebellar tumour excision, a 58 year old post a single right sided stroke and a 41 year old post closed TBI. Only the participant with cerebellar tumour will be discussed. The video game focused on controlling centre of pressure through a virtual reality platform. Three games were developed to fulfil this aim, "Under pressure", "Memory Match" and "Tic-Tac Toe". All three games

encouraged anteroposterior and mediolateral movement with changes to the centre of pressure influencing ability to complete the virtual reality task. A previous pilot study that evaluated the merits of the video games provided positive feedback in relation to enjoyment, difficulty levels and usability (Betker et al., 2006). The games provided varying challenges of speed, direction and range of movement, creating variable intensity based on the participant's needs and abilities. Auditory and visual positive reinforcers were available in the system. The programme of rehabilitation provided to the participant consisted of eight, 45 minute sessions, delivered over a three week period.

Gill-Body et al (1997) utilised a conventional programme of rehabilitation that focused on improving balance and mobility, to ultimately have a positive impact on functional ability. Two participants were included in the study. Participant one was a thirty six year old female, diagnosed with a recurrence of a midline cerebellar pilocytic astrocytoma. She underwent an initial excision of the tumour six years previously, with further surgery required due to recurrence of the same tumour. No change in the histology of the tumour was noted, however, she did require a month of radiation therapy. The associated balance and gait deficits that she experienced were only evident after the second follow-up surgery. The second patient was a forty eight year old male diagnosed with cerebrotendinous xanthomatosis (CTX), a rare autosomal recessive disorder of lipid metabolism but will not be discussed. The main deficits identified by the cerebellar tumour participant were dizziness, unsteadiness when mobilising, impaired upper limb coordination, left sided weakness and reduced balance. The treatment approach adopted included a gait and balance rehabilitation programme that incorporated gaze stabilisation exercises, to maximise stability by improving the patient's ability to effectively utilise visual, vestibular and somatosensory inputs to compensate for the cerebellar deficits. Rehabilitation sessions were provided weekly, for six weeks and lasted between thirty and forty five minutes. Reassessment and progression of the programme was evaluated during these sessions. A home exercise programme was provided encouraging completion at least once a day. An exercise diary was compiled throughout the programme to monitor compliance.

Karakaya et al (2000) implemented a programme of ten sessions of rehabilitation that was provided over a two week period, with patients receiving sessions five days a week. Forty participants were enrolled in the study, twenty individuals with tumours occurring in the

posterior fossa and twenty individuals with tumours migrating into the cerebello-pontine (CP) angle. This area of the posterior fossa is formed from the borders of the cerebellum and pons (Crossman and Neary, 2005) and tumours that invade this aspect of the posterior fossa tend to originate in the internal auditory meatus and invade the CP angle as they increase in size. This is the frequent growth pattern seen in vestibular schwannomas. Presentation and management of this tumour type differs significantly with tumours of the cerebellum, fourth ventricle or brainstem and as a result were not included in this systematic review. The participants of this study received individualised programmes based on presentation, making it difficult to appraise benefit due to the variance across participants.

The paper by Cremer (1998), provided a narrative review of the experience of a fifteen year old male diagnosed with a medullablastoma requiring surgery, chemotherapy and radiotherapy. While the paper outlined that the subject received physiotherapy and occupational therapy during his hospital stay, no details of the utilised programmes were included in the study. The lack of detail prevented the ability to draw conclusions regarding the rehabilitation strategies that may have been used or the potential benefit associated with the chosen techniques.

Four of the five included studies outlined details of the specific programmes provided to the patients (Ada et al., 2009, Betker et al., 2006, Gill-Body et al., 1997, Karakaya et al., 2000). Two studies lacked significant detail making reproducibility of the interventions difficult (Cremer, 1998, Karakaya et al., 2000).

3.8.3.4 Outcome Measures

Outcome measures are measurement tools used to document change over time in individuals to assist with programme evaluation, case management, quality improvements, cost containment and research (Wedge et al., 2012). Comprehensive use of appropriate, valid and reliable outcome measures, assists with ensuring high quality research is conducted. Within the studies in this review, four of the studies used outcome measures to track and monitor change (Ada et al., 2009, Betker et al., 2006, Gill-Body et al., 1997, Karakaya et al., 2000). The measures used in the studies were specific to the aims of the studies.

Ada et al (2009) used the finger nose test (Gagnon et al., 2004) as a measure of elbow dexterity and the 9 hole peg test (NHPT) to look at upper limb dexterity (Mathiowetz et al., 1986). Psychometric properties of the measures were not included. While the researchers identified a small change in the speed and accuracy of upper limb movement in the participant post a two week period of intervention, the changes were only maintained for two weeks duration post the withdrawal of therapy. Betker et al (2006) evaluated parameters extracted from their computerized system including number of falls, range of centre of pressure excursion and centre of pressure of path length. The researchers were able to capture these parameters using incorporated sensors within the system. While the outcome measures are restricted to that measurable using this gaming software, reference is made to comparisons between this balance measurement technique and the sensory organization test, which is a component of the Equitest system, considered the gold standard in balance measurement (Mancini and Horak, 2010). The Berg Balance Scale (Berg et al., 1992), six minute walking test (Schmidt et al., 2013) and the Timed Up and Go (TUG) (Schoene et al., 2013), were conventional measures used. The researchers noted a reduction in the rate of falls in two of the three study participants. Of these two patients, only one was diagnosed with a posterior fossa tumour. Outcome measurement was restricted to the berg balance scale as "difficulties" were cited as limiting the use of the mobility measures. No further explanation was provided on the factors limiting use of these measures. A reduction in falls rate is cited but no Berg Balance re-test data was available. Gill-Body (1997) used a battery of outcome measures in the assessment of balance and mobility function in a single posterior fossa tumour participant. Prior to inclusion in the study the participants received a comprehensive medical examination to ensure suitability for inclusion. The outcome measures administered included the dizziness handicap inventory (DHI) (Jacobson and Newman, 1990), TUG (Schoene et al., 2013), dynamic posturography (Mancini and Horak, 2010) and timed mobility measures (Schmidt et al., 2013) that incorporated variations in speed, head position and degree of visual input. This study also utilised computerised kinematic gait analysis (Olsson et al., 1986). Kinematic gait analysis and dynamic posturography are considered the gold standards in balance and gait assessment, indicating the high quality of assessment methods used in this study. On reassessment at six weeks, improvements were noted in gait, balance and perceived dizziness.

All the measures tracking the changes resulting from a period of rehabilitation in the included studies, outlined improvements at impairment, disability and integration levels. Unfortunately only one study in the systematic review included a follow-up period. This follow-up period was of two weeks duration (Ada et al., 2009). Lack of adequate follow-up combined with lack of controls, limited the ability to draw long term conclusions regarding the benefits of rehabilitation or specific rehabilitation approaches in this population.

3.8.4 Discussion

3.8.4.1 Statement of principal findings

This systematic review investigated and documented rehabilitation practices in the management of deficits in posterior fossa tumour patients. It is the first review to be undertaken to investigate and summarise the rehabilitation practices used in treating these individuals. While the narrative overview confirms that positive benefits were derived from the participants of the studies who received rehabilitation, due to the lack of control groups any conclusions regarding efficacy cannot be made. No conclusions regarding long-term benefits to the included rehabilitation technique could be deduced, due to lack of adequate long-term follow-up within any of the studies. While the execution of this systematic review followed epidemiologic best practice guidelines, the quality of the studies meeting inclusion criteria were all case series. No randomised controlled trial was available for inclusion in the review, highlighting the need for further multi centre prospective cohort studies to examine the impact of rehabilitation exposure in this population.

3.8.4.2 Results in the context of the current literature

Tumours of the posterior fossa are exceedingly rare, particularly within the adult population. The rarity of the condition is reflected in the identification of only five studies, throughout the entire research catalogue, for inclusion in this systematic review. The inclusion criteria limited included studies to individuals with a posterior fossa tumour but other research has investigated deficits of the posterior fossa due to a stroke (Bultmann et al., 2014), Multiple Sclerosis (Prosperini et al., 2011) and Traumatic Brain Injury (TBI) (de Amorim et al., 2014). A systematic review by Martin et al (2009) investigated the effectiveness of physiotherapy interventions in the treatment of deficits of cerebellar dysfunction. This review did not limit inclusion on the basis of a specific pathology.

Participants had varying diagnosis including tumour, TBI, MS and stroke. By basing the inclusion parameters on a specific impairment in contrast to a specific pathology, the researchers were able to identify one randomised controlled trial, one cross sectional study and seven case series for inclusion. Two common studies are included in both systematic reviews (Gill-Body et al., 1997, Karakaya et al., 2000). Similar difficulties with potential reproducibility of the included rehabilitation programmes were experienced due to limited details of the specific programmes. This trend in research publications containing limited details of prescribed programmes, limits the usability and benefit that can be derived by therapists and service users. Follow-up periods were also limited in this study, however, one included study offered a three month follow-up (Folz and Sinaki, 1995), which was significantly longer than the longest follow-up of two weeks offered in this systematic review (Ada et al., 2009). A recent systematic review that investigated approaches in the management of postural disorders associated with cerebellar ataxia identified nineteen studies that focus on rehabilitation (Marquer et al., 2014). Within the included studies only one was identified as containing a definite case of cerebellar tumour. The study identified with this participant is also contained in this systematic review (Gill-Body et al., 1997). Multiple sclerosis and degenerative ataxia were the most frequently included conditions, again highlighting the dearth of available research looking at management of posterior fossa symptoms caused by a tumour.

3.8.4.3 Strengths and weaknesses

This is the first systematic review that has looked at rehabilitation practices in a population of patients with a tumour in the posterior fossa. The methodological process that was undertaken throughout this review was conducted in a systematic and reproducible fashion. A comprehensive search, including five databases and a secondary search of the corresponding reference lists, ensured that the bulk of relevant evidence pertaining to the topic was identified. The search was completed at two points; initially in June 2013 and repeated in April 2015, to ensure the included research was up to date. While every effort was made to comply with epidemiological guidelines when carrying out the searches, the quality of the articles that were identified was of very low methodological quality. All the studies were case series, with limited follow-up, small participant numbers and lacking comparison groups. No randomised controlled trial (RCT) was identified for inclusion. The

poor quality of these five studies, limits the ability to draw robust conclusions from this systematic review.

The specificity of the aim and inclusion criteria of this systematic review provided substantial barriers to the identification of appropriate research articles. As highlighted earlier in the review, the volume of neuro-oncology literature continues to exponentially grow (Khan et al., 2013, Trimble et al., 2015) but, in relation to the posterior fossa the evidence still remains sparse. This review has provided a summary of the available research in relation to rehabilitation of this population. While providing a comprehensive overview of the literature based on sound methodological principles, the quality of the systematic review itself suffers due to the limited historical evidence in relation to this population.

3.8.4.4 Clinical and policy implications

The rehabilitation programmes described within these studies, contained limited details about rehabilitation practices/programmes, making reproducibility and practical implementation difficult. A lack of adequate follow-up across the five studies also limited the ability to formulate conclusions for longer term benefits of the utilised techniques. To ensure transferability of rehabilitation principles into everyday practice they need to be formulated on solid and theoretically sound prescriptive and exercise principles (Swain, 2014). Areas in exercise prescription that have been identified as lacking consistency across research studies include “type of exercise, frequency, duration, repetitions, sets, intensity, progression rules, supervision, individual or group and/or adverse events” (Slade et al., 2014). To overcome this deficit in rehabilitation literature experts in the field of rehabilitation are undertaking an international study to develop consensus on the essential elements required in the reporting of exercise prescription and subsequently develop a standardised method of reporting (Slade et al., 2014). By standardising the reporting in research papers, extrapolation of results will become easier, with more benefits being derived for the service user.

This systematic review has focused solely on a neuro-oncology population. Tumours occurring in the posterior fossa can produce a variety of symptoms due to the potential involvement of several cerebral structures. Given the complexity of this region of the brain and the diversity of tumours based on their histological components (Piccirillo et al., 2014),

proceeding with caution is essential to ensure adequate consideration of confounding factors associated with having a cancer diagnosis of the central nervous system (Buckner et al., 2007).

3.8.4.5 Areas for further research

Ensuring good ethical practice is the cornerstone of any research study (Freedman, 1987), therefore the deliberate withholding of a potentially beneficial treatment approach would breach ethical practice. This ultimately limits the ability to conduct an RCT. This systematic review has highlighted the lack of high quality evidence that is available in this population, identifying the need for future observational research that focuses on prospective, multi-centre cohort studies, with an adequate period of follow-up. The complexity of this population and the changeable nature of brain tumours require a long-term follow-up, to influence a change of practice. Certain neuro-oncology populations have large volumes of high quality research available to assist with clinical decision making (Passier et al., 2012, Roberts et al., 2014). The complexity of this patient cohort and the high degree of mortality associated with tumours of this region of the brain (Strauss et al., 2013), may be a limiting factor in researchers conducting studies that focus on this population.

Two of the studies included in the systematic review used technology as the basis of the rehabilitation programme. Throughout the literature, technology is being incorporated into research and practice (Taylor and Griffin, 2014, Laufer et al., 2014, Meldrum et al., 2012), and offers diversity from routine conventional programmes. Given the increase in technology throughout all aspects of daily living, the incorporation of technology into patient management programmes ensures programmes remains relevant and relatable, for patients (DiDonato et al., 2015).

3.9 Conclusion

Twenty years ago the concept of cancer rehabilitation was “struggling for definition, recognition and direction” (Watson, 1990), but with the increasing numbers of cancer cases and the reduction in mortality rates, cancer rehabilitation has become integral in the management structure of this population. This systematic review highlighted that specifically targeted programmes provided benefits to individuals suffering with symptoms as a result of a posterior fossa tumour. However, the conclusions that can be extrapolated

from this systematic review must be heeded with caution, due to the variation in rehabilitation programmes, lack of comparison groups, limited follow-up periods, small patient populations and variability in subject demographics. More research of higher quality needs to be conducted in this population to allow for optimum rehabilitation strategies to be developed, to maximise functional gains.

Chapter 4: Methodology

4.1 Introduction

Chapter two of the thesis has outlined the anatomical and surgical consequences associated with a tumour of the posterior fossa, while chapter three looked at the role of rehabilitation in the management of this population. The literature reviews have highlighted the limit of specific research available in relation to this complex adult neuro-oncology population. The limit of pre-existing research in this population, limited the resources available on which to establish the methodology for this research project. Subsequently this study was designed to contribute to a foundation in our understanding and management of this complex population. This study aimed to provide scientific information on a complex neuro-oncology population, to assist in the clinical management and future research strategies of this neuro-oncology population.

4.2 Aim of the Research Study

The primary aim of the research was to characterise balance, gait, upper limb dexterity and dizziness in patients, pre and post posterior fossa tumour surgery. The secondary aim was to profile the demographic and tumour characteristics of the study participants.

In this study the experimental hypothesis was that the subjects with posterior fossa tumours would demonstrate reduced balance, reduced gait speed, increased dizziness and reduced upper limb dexterity and quality of life post-operatively when compared with their pre-operative status. The null hypothesis for the research suggested that there would be no difference between pre and post- operative outcomes on assessment of balance, gait, dizziness, upper limb dexterity and quality of life.

A hypothesis was established for each of the outcome measures used in the research project. For the primary outcome measure, computerized dynamic posturography (CDP), it was hypothesized there would be a reduction in measured equilibrium on the sensory organisation test (SOT) when comparing pre and post-surgery results. The proposed hypothesis for the mobility outcome measures, the 10m walking tests, was that there would be a measurable reduction in gait speed between pre and post-surgical testing, for the three test conditions. The hypothesis for dizziness, as measured using the dizziness handicap inventory was an anticipated increase in self-perceived dizziness, as reported by the

participants, pre and post-surgery. The hypothesis for upper limb dexterity, using the nine hole peg test was an anticipated reduction in the speed of completion of the test post-operatively as compared with pre-operatively.

The objectives of the study were:

To establish the impact of surgery on balance, mobility, upper limb dexterity and dizziness in patients, pre and post-surgery, with a tumour of the posterior fossa. Four varying time-points, pre-operatively (T1), post-operatively as an inpatient (T2), six week follow-up (T3) and six month follow-up (T4) were used for patient assessment and data collection.
To characterise the demographic profile of patients admitted to Beaumont Hospital for posterior fossa tumour surgery
To characterise the tumour characteristics of patients admitted for posterior fossa tumour surgery to Beaumont Hospital

4.3 Study Design

This study was a prospective cohort study. The STROBE (Strengthening the Reporting of Observational studies in Epidemiology) standardised reporting guidelines were followed to standardise the conduct and reporting of this research (von Elm et al., 2007).

4.4 Participants

4.4.1 Participant Recruitment

All patients admitted to the Neurosurgical service in Beaumont Hospital for surgery relating to the presence of a posterior fossa tumour were considered as potential subjects for inclusion in the research study. Potential participants were identified by monitoring neurosurgical admission lists, neurosurgical theatre lists and by liaising with the appropriate ward managers and bed managers. Appropriate participants were highlighted to the inpatient neurosurgical physiotherapy service. Patients with the appropriate inclusion criteria were approached by a member of the neurosurgical physiotherapy team, who acted as the gatekeeper. Participants were provided with information leaflets explaining the research project and given a cooling off period to consider their involvement in the study. Written informed consent was obtained when the subject agreed to participate in the research study. Subjects were informed of their ability to withdraw from involvement in the

study at any stage without the need for an explanation. Patients who refused consent to be involved in the research project were advised that refusal would not impact on future care and they would receive normal care as per Beaumont Hospital policy. An anonymous record of all individuals who refused consent or did not meet inclusion criteria was maintained to ensure a complete record of this population of patients over the duration of the study period. Recruitment commenced on the 8th of February 2013.

4.4.2 Inclusion Criteria

Participants were considered eligible for inclusion in the study if they were admitted to Beaumont Hospital for surgery relating to the presence of a tumour in the posterior fossa. Presence of the tumour within the cerebellum, brainstem or floor of the fourth ventricle required confirmation on either MRI or CT, by a consultant radiologist. To ensure no residual deficits secondary to previous surgeries, participants were only included if they underwent first time brain surgery. Any surgical procedure on the brain carried out previously, throughout the lifetime of the individual, resulted in their exclusion from the study. If the individual had received previous brain radiation, they were also excluded due to the potential of developing physical deficits as a result of brain radiation. All participants for potential recruitment to the study were aged 18 or older and able to consent to involvement in the study independently. Potential participants were also questioned as to the presence of, or previous treatment for vestibular symptoms. The individual's medical chart was also consulted to check if there was any evidence of previous medical management for a vestibular lesion. If an individual displayed any difficulty with the consent procedure due to altered Glasgow Coma Scale (GCS), they were excluded as potential participants. Individuals provided written informed consent for involvement in the study. Individuals had to be able to mobilise for inclusion in the study but individuals who mobilised with the use of a gait aid were still offered the opportunity to be involved in the study. Ability to stand for approximately twenty seconds to allow testing on the Equitest (primary outcome measure) was also a criterion for inclusion. Due to the use of written questionnaires and outcome measures in English, fluency in written and spoken English was required.

4.4.3 Exclusion Criteria

Patients were excluded from consideration for the study if they had a neurosurgical opinion and assessment while an inpatient that did not warrant a surgical intervention. Individuals unable to provide written, informed consent or unable to comprehend written or spoken English were also excluded. Inability to complete the testing battery resulted in exclusion. Individuals with a tumour originating from the internal auditory meatus were excluded as this is the common site of origin of vestibular schwannomas, which display similarities in presenting features but differ in management to the population of interest. The study cohort was an adult population, so participants under 18 years of age were excluded.

4.5 Sample Size

Beaumont Hospital is the National Neurosurgical centre in Ireland with 2,455 admissions and 25,339 bed days utilised by the neurosurgical service in 2013 (Beaumont Hospital Annual Report, 2013) . Over a five year period, ranging from 2007 to 2011 inclusive, 114 patients were admitted to Beaumont and had surgery as an inpatient due to the presence of a posterior fossa tumour, with an average annual admission rate of 23. Based on the above figures it was assumed that the number of patients potentially meeting inclusion criteria would be reflected in these numbers. Recruitment was also dependent on patients consenting to being involved. Assuming 50% of the potential participants would decline involvement, the study aimed to recruit a minimum of twelve participants over an eighteen month period. Pre-existing research data was unavailable on which to formulate a scientific calculation.

4.6 Ethical Considerations

An application for ethical approval was initially submitted for consideration by Beaumont Hospital Medical Research Ethics Committee on 25th of October 2012. On receiving feedback from the ethics committee, minor modifications were required to the patient information leaflet. On resubmission of the amended patient information leaflet, ethical approval was received on 20th of December 2012. A copy of the Ethics approval is available as appendix eleven. An amendment form was submitted to the Beaumont Hospital Ethics Committee on 29th January, relating to a modification in the testing procedure. Addition of the nine hole peg test (NHPT), a functional measure of upper limb dexterity was included in the testing battery post discussion with a neurosurgeon (SMcN). Approval for inclusion of the NHPT was

received on the 8th February 2013 from Beaumont Hospital Ethics Board. A copy of the Ethics approval is available as appendix twelve.

All potential participants were provided with a copy of the patient information leaflet when approached by the gatekeeper, if they indicated an interest in considering involvement in the research study. A copy of the information leaflet is available as appendix thirteen. The aims and objectives of the research were outlined to the patient at this time and participants were informed of the voluntary nature of the study. Participants were also advised that refusal to participate would not impact on any future care they would receive while a patient in Beaumont Hospital. Verbal consent was obtained to ensure the participant was happy to be approached by the principal investigator (PI). The participant was provided with a cooling off period of at least one hour to ensure adequate time to evaluate their potential involvement in the study. The patient was advised of their ability to withdraw from the study at any point, without explanation and it would not impact on their future management.

The PI approached the participant once verbal consent was obtained to do so. Any outstanding questions requiring clarification were discussed at this point. The withdrawal process from the study was also re-clarified at this point. Signed, informed consent was obtained from the subject. One copy was placed in the subject's medical chart, one copy was provided to the subject and one copy was retained by the PI. A copy of the consent form is available as appendix fourteen.

There was no identifiable personal information collected on the data collection form used to gather participant information. A unique identification code was assigned to each participant and was used to identify participant data. The identification codes and subjects' names were stored on a password protected spread sheet, to which only the PI had access. All written documentation was kept in a locked filing cabinet in the physiotherapy department to which only the PI had access. Data was stored on a hard drive which was password protected. The collection, storage and use of participant data was carried out in accordance with the Data Protection Act (1998). Prior to commencement of the study each neurosurgical consultant was contacted by email informing them of the study and was provided with a copy of the finalised protocol. A letter was forwarded to each consultant

informing them of their patient's involvement in the study if they consented to participation. A copy of the consultant letter is available as appendix fifteen. A letter outlining the participant's involvement was also forwarded to their General Practitioner (GP). A copy of the GP letter is available as appendix sixteen.

A small number of potential risks associated with involvement in the research study were identified. A fall was perceived as being a potentially high risk consequence due to the challenging nature of the balance testing, involved in the assessments. To minimise the risk of a fall, all participants were closely supervised throughout the testing procedure by the PI and if any adverse event occurred the testing was ceased and the treating neurosurgical team were contacted and advised of the event. Neck pain was also considered a potential risk due to the presence of a sub-occipital post-operative wound. As the subjects were requested to move their head from side to side during the testing, potential post-operative wound discomfort may have been experienced. To minimise this risk, the patient's cervical range of movement was tested prior to conducting the walking tests. The patient was instructed to carry out the movements of the head and neck within comfortable limits. If no comfortable limits were identified the walking tests involving the horizontal head turns were excluded from the testing battery. If increases in neck pain were identified post testing, the ward was contacted regarding the administration of pain relieving medication. Increase in the levels of dizziness was also identified as a potential risk of inclusion in this study. If subjects reported an increase in their levels of dizziness post assessment that did not settle, the treating neurosurgical team was contacted. Fatigue was also identified as a risk due to the impact of surgery and the number of assessments being conducted. Opportunity to rest between each test was provided for each participant and any further request for rest periods was provided. No adverse events occurred at any time-point, during the testing of participants.

4.7 Procedure

When a patient was admitted to one of the neurosurgical wards in Beaumont Hospital and met the inclusion criteria, they were approached at this point by the gatekeeper to outline the research study. A cooling off period of one hour was provided and they were given the information leaflet to assist with decision making regarding consent. If the patient consented to being approached by the PI, the study was further discussed prior to decision

making. If the patient wished to be involved in the study written informed consent was obtained. The individual's medical chart was assessed to obtain baseline demographic data and information relating to their admission history. A copy of the data collection sheet is available as appendix 17. Beaumont Hospital PACS system (online radiological system) was accessed to confirm a tumour of the posterior fossa on CT or MRI as confirmed by a consultant radiologist. A time was then arranged to execute the assessments that was agreeable to the participant, in the physiotherapy department.

The assessments and outcome measures were conducted at four consecutive time-points (Tp) during the study. The SOT testing procedure, of the CDP Equitest system, was the primary outcome measure used in the study. The composite score of the SOT was the primary endpoint utilised in the study. A table of the testing procedure at each time-point is available as appendix 18.

Tp1: Pre-operatively- This was the initial battery of testing that was completed prior to the individual undergoing their neurosurgical procedure. The number of days prior to surgery that this testing occurred varied between participants due to several factors. Access to participants varied due to absence from the wards due to radiological demands and consultations with a variety of healthcare professionals. At this stage of the testing procedure the testing protocol consisted of collecting demographic data, completion of the SOT component of the Equitest, 10 metre walk tests, the Nine Hole Peg Test (NHPT), Linear Analogue Scale Assessment (LASA) and the dizziness handicap inventory (DHI).

Tp2: Post-operatively as an inpatient- The post-operative testing battery was completed at the first opportunity that the participant reported feeling able to engage. Given the nature of the presentation, the number of days post-operatively, that this testing was completed varied between participants. The testing protocol at this point included the SOT component of the Equitest, 10 metre walk tests, NHPT, box scale for pain, and DHI.

Tp3: Post-operatively at 6 week review – This stage of the testing was completed to coincide with the patient's six week clinic review with the treating neurosurgeon. The testing protocol at this stage of the study included the SOT component of the Equitest, 10m walk tests, NHPT, DHI and box scale for pain.

Tp4: Post-operatively at six months – This stage of the testing was completed by phone follow-up in which subjective measures were completed over the phone with the participants. The testing protocol included the LASA, DHI and box scale for pain.

A copy of the data collection checklists utilised at each Tp, are available as appendix 19, 20, 21 and 22.

4.8 Assessments

4.8.1 Demographics

Demographic information for each of the participants was collected from the medical chart, once written informed consent was obtained. Any missing information from the medical chart was supplemented by discussion with the participant. This included information on gender, age and mobility status. A comprehensive history of presenting features was obtained. This included the presence of nausea, vomiting, dizziness, vertigo, tinnitus and oscillopsia. This participant information was collected initially, in conjunction with T1 testing protocol and was not repeated during the other testing time-points. A record of the number of days each participant was an inpatient in Beaumont Hospital was also collected, at discharge. The GCS was also recorded at admission and any change in the same throughout the inpatient stay was noted, to monitor clinical deterioration. If the participant required an intensive therapy unit (ITU) admission during their inpatient stay this was also captured. All testing completed during the course of the research project was executed by the PI (KM), to ensure consistency and reduce the risk of bias. The majority of the demographic data was collected at T1 but supplementary information was gathered at each of the time-points. At T2, data relating to the surgery and the tumour was collected, at T3 information relating to radiation and chemotherapy and at T4 data relating to general well-being and current functional status was collected.

4.8.2 Computerized Dynamic Posturography (CDP)

Computerised dynamic posturography is a quantitative method of measuring upright balance function under a variety of simulated balance conditions (Jacobson et al., 1993), and is considered a gold standard objective measure in balance assessment (Mancini and Horak, 2010). The Equitest system contains three programmes designed to challenge aspects of

balance including the motor control test (MCT), sensory organisation test (SOT) and adaption test (AT).

Platform posturography, in the clinical setting was developed to clarify the nature of motor coordination problems associated with vestibular impairments and other sensorimotor deficits (Di Fabio, 1995). Nashner and Peters (1990) developed the sensory organisation test (SOT) based on the hypothesis that "disruption to the gravitational reference (low-frequency otolith feedback) would create postural instability if visual and somatosensory inputs were not available as redundant systems to control balance" (Nashner, 1971, Nashner, 1972, Di Fabio, 1995). The SOT in the clinical setting is used to evaluate postural sway in six conditions, in which visual and somatosensory cues are absent or altered (Herdman, 2007). While considered a gold standard in balance assessment several limitations exist. An extensive collaboration of experts in balance and motion identified poor sensitivity and specificity of CDP in its ability to identify and quantify postural and balance deficits (Kingma et al., 2011). A retrospective review of the SOT and its ability to detect balance deficits in a population with central nervous system balance deficits, reported 100% sensitivity in identifying balance deficits (Keim, 1993). In a review of the learning effects of repeated administration of the SOT in a healthy, young population, Wrisley et al (2007) identified a fair to good test-retest reliability of the SOT composite score, from session one to two, with an average of 1.7 ± 0.9 days between testing, highlighting a .67 intra-class correlation co-efficient (ICC). Within the same study, the investigators identified an eight point change in the composite score as a clinically meaningful improvement in equilibrium. The researchers identified this score as sufficient to counteract the potential of a learning effect, making an eight point change in score attributable to the associated intervention. While the diagnostic abilities of CDP and the SOT have been called into question (Baloh et al., 1998), the ability of the SOT to track changes of balance function over time have been proven, emphasising its ability to monitor the impact of rehabilitation and medical interventions (Di Fabio, 1995).

Postural sway is measured in the SOT by manipulating visual and somatosensory feedback, with the aim of evaluating the person's postural stability (Mirka and Black, 1990). The SOT is administered with a computerized system using a movable dual force-plate and a movable visual screen (Equitest) (Ford-Smith et al., 1995). Varying degrees in body sway compared to

maximum known limits, measured during the six sensory conditions determines the person's ability to organize and select the appropriate sensory information to maintain postural control (Nashner and Peters, 1990). Each condition has three, 20 second trials. In condition one, the participants stand still with eyes open. No alteration to sensory stimulation is provided in this testing condition. Visual stimuli are removed in condition two by instructing the subject to close their eyes. In condition three, visual stimuli are altered by moving the visual screen with the subject's anterior/posterior sway, thus maintaining the visual field a constant distance from the subject's eyes. This is referred to as "sway referencing" (Nashner et al., 1982). In condition four, proprioceptive stimuli are distorted by rotating the force platform with the subject's sway, while maintaining a constant angle at the ankle joint. Condition five, removes visual input by eye closure and alters proprioceptive stimuli, due to sway referencing. In condition six proprioceptive and visual stimuli are both altered by moving the platform and sway referencing (Ford-Smith et al., 1995). During conditions four, five and six, the vestibular system is believed to be the main sensory control system (O'Neill et al., 1998).

The Equitest system was used to administer the SOT protocol in this research project. The equipment consisted of a movable dual force-plate, a movable visual screen and overhead safety bar with safety straps. The dual force-plate consisted of two 9 x 18 footplates connected by a pin joint. The two footplates have four force transducers mounted symmetrically under the footplates on a supporting centre plate and a fifth transducer is bracketed to the centre plate directly beneath the pin joint. The force transducers are placed so that when a subject stands with ankles centred over the placement strip on the dual force-plate, with feet an equal distance laterally from the centre line, his or her centre of gravity (COG) is positioned directly above the intersection of the X and Y axis (Ford-Smith et al., 1995).

Figure 4a Participant within the Equitest system

Within the testing battery, the SOT was used to measure the participant's equilibrium pre-surgery (T1), post-surgery (T2) and at clinic review (T3). The testing procedure followed the SOT pre-programmed Equitest protocol. The participant was instructed regarding the testing procedure prior to commencing testing. The participant's height was also measured and input to the system along with age, to allow comparison with computed normative data. Each trial is scored separately with equilibrium scores expressed as a percentage ranging from zero to one hundred. Equilibrium scores nearer one hundred indicated reduced antero-posterior (AP) excursion. AP excursion is a measure of sway in the antero-posterior direction of the participant's centre of gravity in relation to the ankle position (Nashner et al., 1982). The trial was stopped if the subject took a step, opened their eyes, stepped off the force platform or grabbed an object to maintain upright stance. Interrupted trials were considered a fall and scored zero. A composite score was automatically calculated by the equipment based on normative data and was used for statistical analysis.

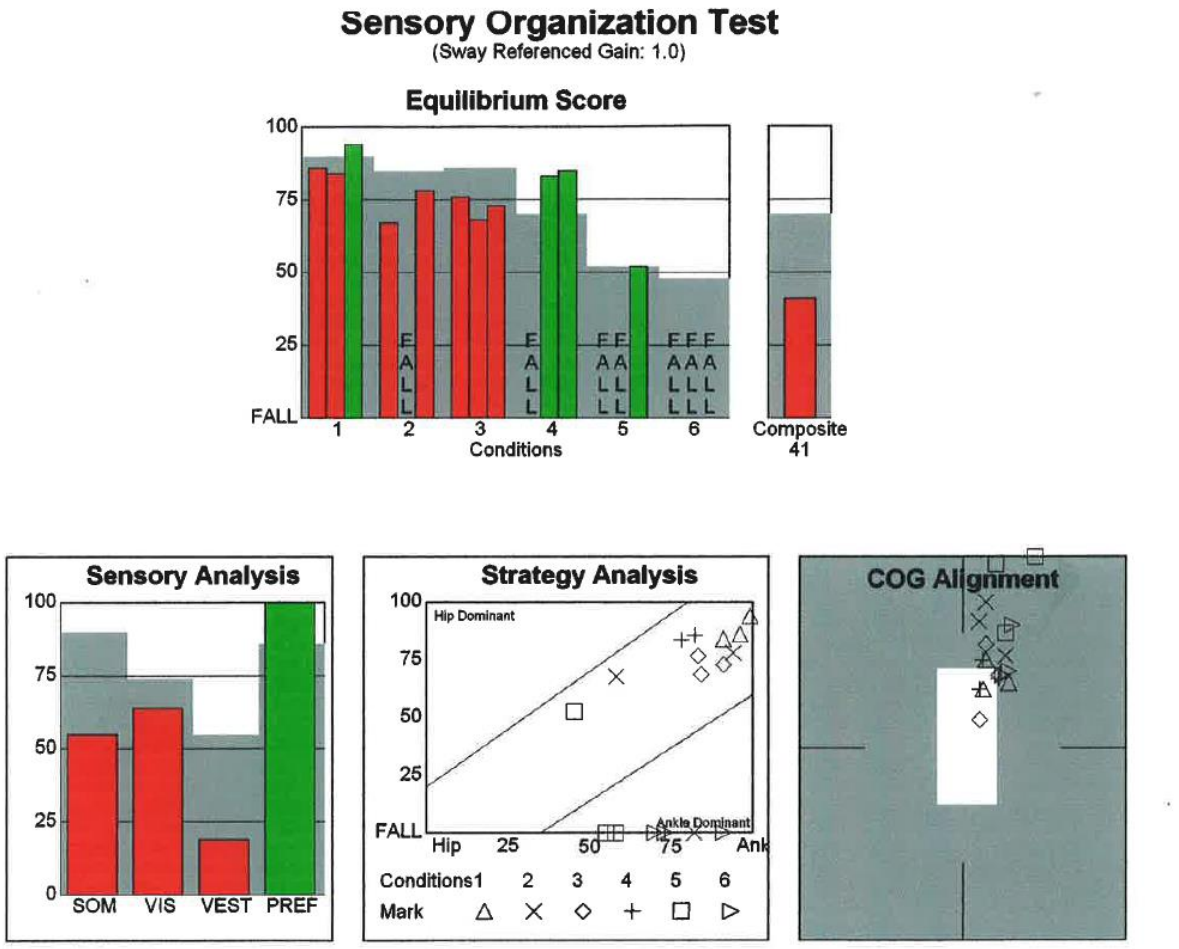


Figure 4b Computerized output of SOT for a study participant.

The output provides a graphical representation of the score for each trial and the computer generated composite score. Graphical representation is also provided for sensory analysis, ankle and hip strategy analysis and alignment of the centre of gravity. The red areas represent trials where the individual scored lower than age matched normative data. Green areas indicate scores that are equal or higher than that of age matched normative data.

4.8.3 10m Walk Test

Individuals with balance or vestibular disorders frequently demonstrate gait disorders, report postural instability and fall more frequently than individuals without vestibular dysfunction (Marchetti et al., 2008). Typically, clinical features identified in individuals with infra-tentorial tumours revealed ataxic gait including widened base, unsteadiness, irregularity of steps and veering to one side (Palliyath et al., 1998). Laboratory studies in individuals with cerebellar disease revealed that cadence and step length are significantly lower, whilst step width, stance phase and outward rotation of feet are significantly increased in cerebellar patients compared to normal subjects. As a result of this reduction in step length and cadence, a diminution of gait velocity is also observed (Stolze et al., 2002). Walking speed has been shown to be a key factor in determining rehabilitation needs and discharge location and has the potential to predict future functional decline and fall risk (Peters et al., 2013).

Given that irregularities of gait velocity and cadence have been identified in individuals with involvement of the cerebellum (Ilg et al., 2007, Stolze et al., 2002), a simple 10 metre walk test was employed to measure these temporal gait parameters, in the participants with posterior fossa involvement. Three varying testing conditions involving the 10m walk test were used; self-selected walking speed, maximum walking speed and walking with horizontal head turns.

In a study investigating the impact of locomotion speed on gait variability in individuals with vestibular and cerebellar deficits, temporal gait variability was identified in both populations (Schniepp et al., 2012). In patients with cerebellar ataxia, variability was increased during slow (8.4 ± 5.3%, $P < .01$) and fast (7.9 ± 6.4%, $P < .01$) walking speed but was normal during preferred walking speed. In a review of temporal and spatial gait parameters in individuals with and without balance and vestibular disorders, a significant decrease in gait speed for several conditions of the Dynamic Gait Index, including horizontal head turns was identified (Marchetti et al., 2008).

The ease of administration of the 10m walk test in the clinical setting has made it a commonly chosen measure to monitor gait speed. The psychometric properties of the measure have been investigated in several populations. Test retest repeatability has been

shown to be excellent at both self-selected and maximal walking speeds, in a healthy adult (ICC 0.93, ICC 0.91) (Bohannon, 1997) and chronic stroke (ICC 0.94, ICC 0.97) (Flansbjer et al., 2005) population. In the same cohort of chronic stroke participants, Flansbjer et al (2005) identified a standard error of measurement of 0.07m/s at a self-selected comfortable speed and 0.08 m/s at maximal walking speed. In the clinical environment a variation in clinically meaningful, gait speed changes have been identified across differing cohorts. In an elderly population, 0.05 m/s was classified as a small meaningful change in gait speed and 0.13 m/s a substantial change (Perera et al., 2006). The researchers identified similar trends in a stroke population with 0.06 m/s classified as a small change and 0.14 m/s classified as substantial (Perera et al., 2006). In a chronic TBI population, a change of 0.15 m/s at a self-selected pace and 0.25 m/s at maximal walking speed was considered clinically meaningful (vanLoo et al., 2004).

Each participant completed 3 consecutive trials for each walking test, for a total of 9 walking trials. An average gait speed was then calculated from the three trials. The testing procedure used was identical to that outlined in previous studies (Peters et al., 2013). A copy of the testing protocol is available as appendix 23. Walking speed was measured using a stopwatch, starting the stopwatch as soon as the participant's lead leg crossed the first marker and stopping it when the participant's lead leg crossed the second marker. The PI performed all stopwatch measurements to prevent introducing inter-rater variability. Participants were provided the opportunity to take rest breaks as needed throughout the testing session but no participant required a break.

4.8.4 Nine Hole Peg Test

The Nine Hole peg test (NHPT) is one of the most frequently utilised assessments for the measurement of upper limb dexterity (Oxford Grice et al., 2003). It is a timed test in which nine pegs are inserted and removed from a pegboard containing nine holes (Poole et al., 2005). Age related normative data as well as a standardised testing procedure have been established for consistency of testing (Mathiowetz et al., 1985). Inter-rater and test–retest reliability of the most widely-used, commercially available version of the Nine Hole Peg Test has been established (Oxford Grice et al., 2003) and was found to be very high (right = .984, left = .993). The standard error of measurement, in a stroke population of varying time since onset was 29 seconds (Chen et al., 2009) and 1.02 seconds for the dominant hand in a

Parkinson's disease population (Earhart et al., 2011). Within the same studies, a minimal detectable change of 32.8 seconds in the stroke population (Chen et al., 2009) and 2.6 seconds for the dominant hand in the Parkinson's disease population (Earhart et al., 2011), was identified. The merits of the NHPT as a quick, easy to administer and reliable measure of upper limb dexterity has been established (Mathiowetz et al., 1985, Smith et al., 2000). Its predictive role of upper limb deficits of dexterity has been recognised by its inclusion in the NIH Toolbox (Wang et al., 2011). The NIH toolbox initiative was developed to provide "a standard set of concise, well validated measures that will be available in English and Spanish for longitudinal or epidemiological studies and also for prevention or intervention trials of people aged 3–85 years" (Gershon et al., 2010).

The testing procedure utilised in this study was that outlined by Mathiowetz et al (1985) and replicated by Oxford-Grice et al (2003). Each participant was instructed to centre the pegboard directly in front of him or her, oriented such that the shallow dish was on the participant's dominant hand side and the peg holes on the non-dominant side. Instructions for the test were given as per the standard instructions (Mathiowetz et al., 1985), along with a brief demonstration. A copy of the standardized testing procedure is available as appendix 24. Participants were given the opportunity for a practice test prior to the actual test, commencing with the dominant hand and then the non-dominant hand. The actual testing procedure was then completed in the same format with the dominant hand first followed by the non-dominant hand. The tests were timed, with a stopwatch, from the moment the participant touched the first peg until the moment the last peg hit the dish. The test was then repeated for the non-dominant hand using the same testing method, with the pegboard rotated such that the dish was in front of the non-dominant hand. All participants were tested using this procedure. In the event that the participant dropped a peg or the trial was interrupted in any way, the evaluator cued the participant to stop and a new trial was initiated (Oxford Grice et al., 2003). All trials of the NHPT, at all the testing time-points were completed by the PI, for consistency.

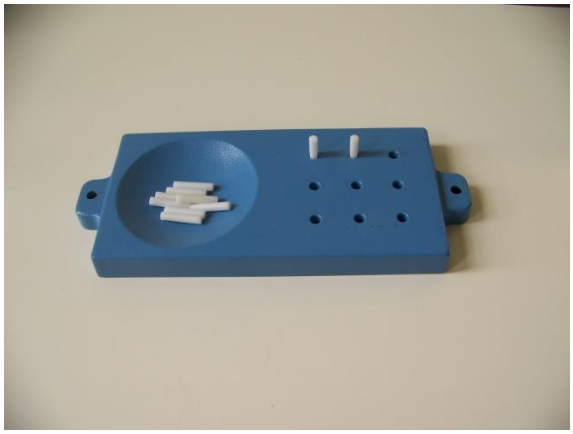


Figure 4c NHPT board

4.8.5 Dizziness Handicap Inventory

The Dizziness Handicap Inventory (DHI) (Jacobson and Newman, 1990) is a self-perceived measure of disability attributed to vestibular dysfunction (Herdman, 2007). The subjective perception of vertigo and dizziness is believed to be influenced by the patient's personality, anxiety with regards to unforeseeable recurrence, associated symptoms and the unpredictable evolution of the underlying disease (Duracinsky et al., 2007). The scale consists of 25 questions that are classified into physical, functional and emotional subgroups with the aim of evaluating the impact of dizziness on the way a patient functions in everyday life (Jacobson and Newman, 1990). The scale is scored by providing four points for a "yes" response, two points for a "sometimes" response and zero for a response of "no". The scoring sequence ranges from zero to one hundred with zero indicating no perceived disability and 100 indicating a maximum perceived disability (Herdman, 2007). Good internal consistency reliability was demonstrated when the scale was administered to 106 consecutive subjects (Jacobson and Newman, 1990) but the construct validity of the scale was called into question as only item total correlations have been studied. A factor analysis study carried out on a Spanish population of 337 patients identified three factors that differed from the original publication including, "vestibular disability", vestibular handicap" and visio-vestibular disability". The discrepancies identified between the English and Spanish version of the scale highlight the potential for error and the inability to ensure validity of the measure in alternate languages. The standard error measurement, in a population with peripheral and central vestibular pathology, was identified as 6.23, with an 18 point change in the scoring required to signify a minimal detectable change in the individual's self-

perceived dizziness handicap (Jacobson and Newman, 1990). A copy of the scale is available as appendix 25.

In an article reviewing 74 studies relating to the DHI (Mutlu and Serbetcioglu, 2013) it was concluded that self-reported measures provide unique information in the management of the dizzy patient. The DHI was reported as the most widely used self-reported measure of dizziness and has been translated into fourteen languages making it widely recognised and accepted.

4.8.6 Box scale for pain

Due to the risk of post-operative pain associated with the participants in this study, a measure of pain was included in the testing battery at time-points two, three and four. The numeric rating scale (NRS) involved asking participants to rate their pain intensity by selecting a number on a scale from 0–10 (11-point scale) by filling in a questionnaire or stating verbally a numerical level (Mannion et al., 2007). The box scale is a slight variation , where each number (e.g. 0−10) is written in a box and participants are asked: “If a zero (0) means ‘no pain’ and a ten (10) means ‘pain as bad as it could be’, on this scale of 0−10, what is your level of pain? Put an “X” through that number”(Jensen et al., 1986).

In a comparison study of the visual analogue scale (VAS), numeric rating scale (NRS) and the verbal rating scale(VRS), the NRS was found to provide interval level data and was as sensitive as the VAS (Williamson and Hoggart, 2005). The scale is considered easy to administer and record. In a study examining the validity of a verbally administered 0-10 NRS, the correlation between the VAS and the NRS was found to be strong and statistically significant in a mixed oncology population ($r = 0.847$, $p < 0.001$) (Paice and Cohen, 1997). In a population of post-surgical patients of varying pathology, 35% reduction on the numeric pain rating scale indicated minimal relief, 67% moderate relief and 94% complete relief (Sloman et al., 2006). In a population of limb and neck pain patients, a change of three points on the scale was required for a meaningful change (Stratford and Spadoni, 2001).

The validity of verbal delivery of the NRS, for use in this study was important, as the measure was administered by phone by the PI at T4, as part of the six month follow-up testing battery. Administration of the box scale for pain was conducted in person with the participant at T2 and T3 in the physiotherapy department of Beaumont Hospital so the

participant was familiar with the measure being administered by phone at T4. A copy of the Box scale for pain is available as appendix 26.

4.8.7 Linear Analogue Scale Assessment (LASA)

The LASA is a brief quality of life measure that has been validated for used in the neuro-oncology population (Locke et al., 2007). Specific domains include physical well-being (i.e., fatigue, activity level), emotional well-being (i.e., depression, anxiety, stress), spiritual well-being (i.e., sense of meaning, relationship with God), and intellectual well-being (i.e., ability to think clearly, concentrate). An item for overall QOL is also included. The Likert scales run from 0 (as bad as it can be) to 10 (as good as it can be). Thus, higher ratings suggest higher QOL. The LASA was completed as part of the testing battery pre-operatively and at six months follow-up. Failure to include the LASA as a component of the testing battery at the other two testing time-points was aimed to reduce participant burden by collecting the quality of life data at the most appropriate time-points, to highlight the long-term quality of life, as a consequence of the surgery. A copy of the LASA is available as appendix 27.

4.8.8 Tumour specific information

Information relating to the tumour and the associated surgery was captured. Initial presenting information was gathered once consent was obtained and collected from the participant's medical chart and the online computerised radiology system (PACS) in Beaumont Hospital. Information included, the exact location of the tumour, size, histology, presence of midline shift, presence of hydrocephalus, presence of mass effect, surgical procedure undertaken and extent of the surgical resection. Tumour size was determined by the maximum diameter of the tumour, in any one direction, as classified by the treating neuro-radiologist. Data relating to the surgical intervention and tumour histology was captured post-operatively, prior to the participant's discharge from hospital. A record of need for future radiotherapy or chemotherapy was also captured.

4.9 Statistical Analysis

Data was analysed using STATA (version 13). Descriptive statistics, with graphical and tabulated data representation were utilised throughout the study. A narrative representation of study outcomes was also provided to monitor change over time in the cohort and the impact of surgery on outcomes.

The use of inferential statistics was restricted in the study to track changes over time due to the small cohort. Loss to follow-up and incomplete datasets further restricted choice of statistical analysis used. The limited number of study participants restricted the complexity of statistical analysis completed. Statistical analysis of the research data was completed in conjunction with a statistician.

4.10 Conclusion

Chapter four has categorized in detail the study methodology followed in the execution of this research project and the testing procedures utilised. The results of the study are presented in chapter five.

Chapter 5: Results

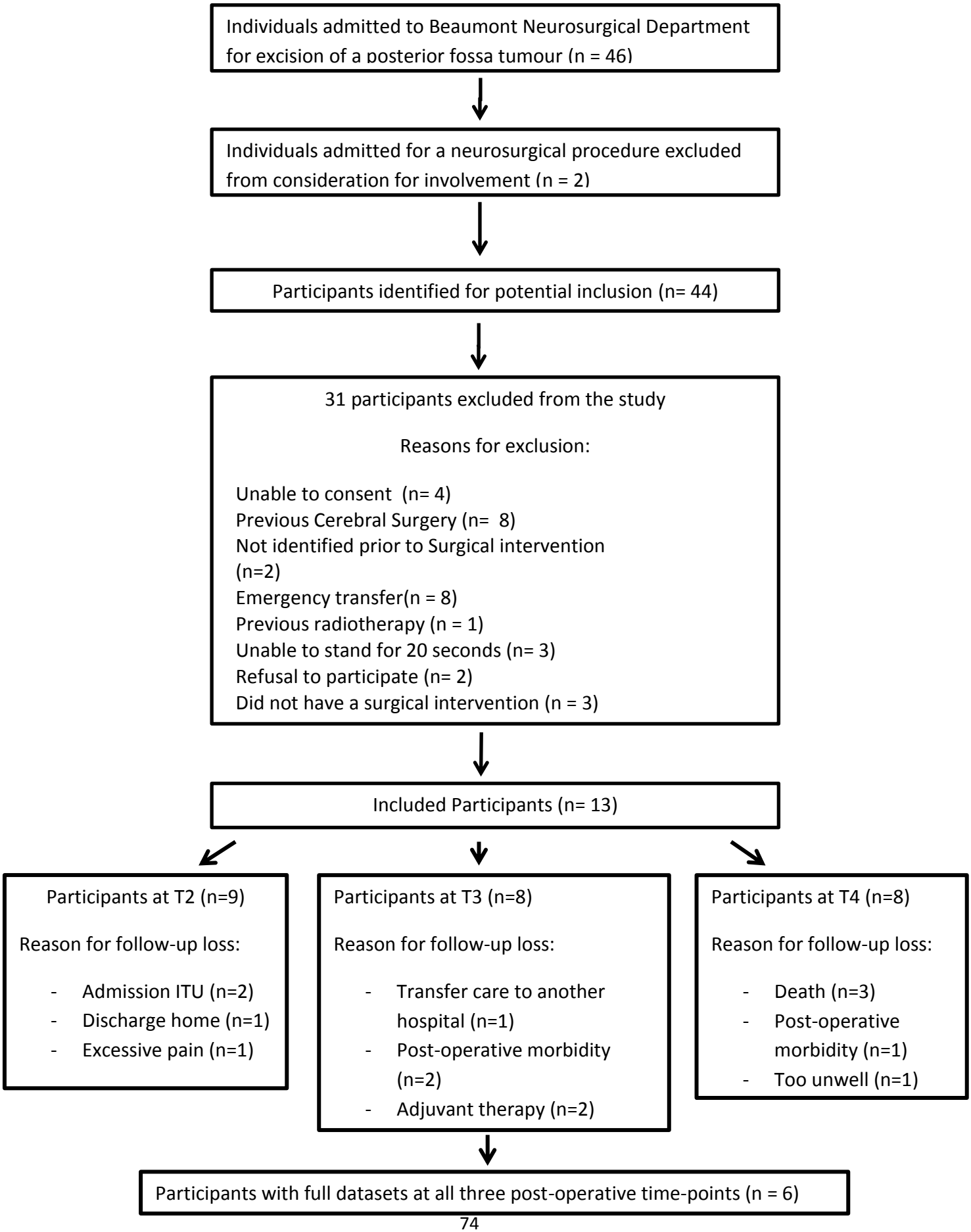
5.1 Introduction

The aim of the study was to establish the impact of surgery on balance, mobility, upper limb dexterity and dizziness in patient's pre and post-surgery for the presence of a tumour of the posterior fossa. Secondary aims of the study included characterising the demographic and tumour profiles of the cohort of patients admitted to Beaumont Hospital for posterior fossa tumour surgery. The experimental hypothesis was that the subjects with posterior fossa tumours would demonstrate reduced balance, reduced gait speed, increased dizziness and reduced upper limb dexterity and quality of life post-operatively when compared with their pre-operative status. The null hypothesis for the research was that there would be no difference between pre and post- operative outcomes on assessment of balance, gait, dizziness, quality of life and upper limb dexterity.

5.2 Participant recruitment

Thirteen participants were recruited for involvement in this study. The recruitment process commenced on 8th February 2013, once ethical approval was received from Beaumont Hospital Ethics Committee, and concluded on 5th June 2014 once the desired recruitment sample size had been achieved. Consecutive patients admitted to the neurosurgical department of Beaumont Hospital for surgery due to the presence of a tumour located in the posterior fossa were considered for inclusion in the study. Inclusion was dependent on fulfilling the inclusion criteria and providing informed, written consent to participate in the research study. During the recruitment period, 46 individuals were admitted to Beaumont Hospital for a surgical procedure due to the presence of a tumour of the cerebellum, brainstem or fourth ventricle. These figures were sourced from the Beaumont Hospital HIPE (hospital inpatient enquiry) system that tracks and codes patient admissions to the hospital, based on diagnosis. Flow of participants through the study is demonstrated in figure 5a (overleaf).

Figure 5a Flow of participants through the study



5.3 Description of the study group

The study sample consisted of eight females (62%) and five males (38%). The mean age of the sample was 48.8 ± 15.7 years. Participant ages ranged from 21 years to 77 years. The female participants in the study had an average age of 49 years with males having an average age of 48.6 years. While both groups had the same average age, the male group of participants contained both the youngest and oldest participants (21 years and 77 years) recruited to the study. Of the recruited participants, all displayed a Glasgow Coma Scale score of 15/15 (100%), as measured by the treating nursing staff on the day of approach by the gatekeeper regarding potential inclusion. At admission to hospital twelve participants were independently mobile without the use of an aid (92.3%) and one participant used a zimmer-frame (7.7%), at baseline. Eleven participants were right hand dominant (84.6%) and two were left hand dominant (15.4%). The demographic data of the study participants are summarised in table 5a (below).

Table 5a Demographic data of participants

Variable	Subjects (n=13)
Age (Mean and SD)	48.8 ± 15.7
Gender (n)	8 Females 5 Males
GCS at Admission (n)	GCS 15/15 = 13
Mobility Status (n)	Independent = 12 Zimmer frame = 1
Hand Dominance (n)	Right = 11 Left = 2

5.4 Excluded Participants

During the period of recruitment 31 participants were excluded from inclusion in the study for varying reasons. The most common reason for exclusion from the study was due to a previous brain operation and eight subjects (25.8%) were excluded as a result. Four individuals (12.9%) were unable to provide consent, secondary to a low GCS, eight participants (25.8%) were transferred for surgery as a medical emergency thus were unable to engage in the recruitment process, one individual (3.2%) had previous radiotherapy to the brain, three participants (9.7%) were unable to stand for testing, two individuals (6.5%) refused to participate in the study, three individuals (9.7%) did not have a surgical intervention and two individuals (6.5%) were not identified early enough pre-surgery to complete the recruitment and testing process. The excluded participant data are summarised in figure 5a, page 74.

5.5 Loss to follow-up

Thirteen participants were recruited for inclusion in the research study. All participants completed the objective testing at T1, pre-operatively. One participant, (P6) did not return the subjective measures, DHI and LASA to the PI post completion and the data was not included. Follow-up with the participant (P6) regarding the pre-operative assessments was not possible due to significant post-operative morbidity which prevented subsequent testing.

At T2, nine participants (69%) completed the testing protocol with four participants not included at this time-point. Two participants (16%) were admitted to ITU requiring intubation and ventilation, one participant (8%) was discharged home prior to completing the testing battery and one participant refused to engage with testing due to excessive post-operative pain levels (8%).

At T3, eight participants completed the testing protocol with five participants not included at this time-point. Two participants (16%) had significant post-operative morbidity and were unable to participate in testing. These two participants were the same two participants that had been admitted to ITU post-operatively. Two participants (16%) were receiving adjuvant chemotherapy or radiotherapy and were not eager to engage at that point and one

participant (8%) had his care transferred to local services in Galway and was unable to return to Dublin.

At T4, eight participants completed the testing protocol with five participants not included as this time-point. Three participants (24%) were dead at six month follow-up, one participant (8%) had significant post-operative morbidity that prevented engagement and one participant (8%) was too unwell at six month follow-up to participate. The mortality and morbidity of the study cohort is presented in figure 5b (below).

Table 5b Study Outcomes for mortality and morbidity

Outcome	**Time-point**			
	T1	**T2**	**T3**	**T4**
Mortality	0	0	0	3
Morbidity	0	2	2	2

Footnote: Numbers equating to the number of individuals unable to complete testing at a particular time-point, due to death or significant morbidity

Table 5c Testing protocols completed by each participant during the research project

Participant	T1	T2	T3	T4
P1	√	√	√	×
P2	√	√	√	√
P3	√	√	×	√
P4	√	×	×	×
P5	√	√	√	√
P6	√¶	×	×	×
P7	√	×	√	√
P8	√	×	√	×
P9	√	√	×	×
P10	√	√	√	√
P11	√	√	×	×
P12	√	√	√	√
P13	√	√	√	√

√ = Completed testing battery

× = Did not complete testing battery

¶ = Did not complete LASA

5.6 Tumour Characteristics

All participants included in the study subsequently had a surgical intervention secondary to a tumour in the posterior fossa of the cranium. Three tumours were located in the fourth ventricle, two in the cerebellar vermis, eight within the cerebellar hemispheres and none were within the brainstem. The size of the tumours varied from 2.5cm to 4.5cm and is illustrated in figure 5b (below).

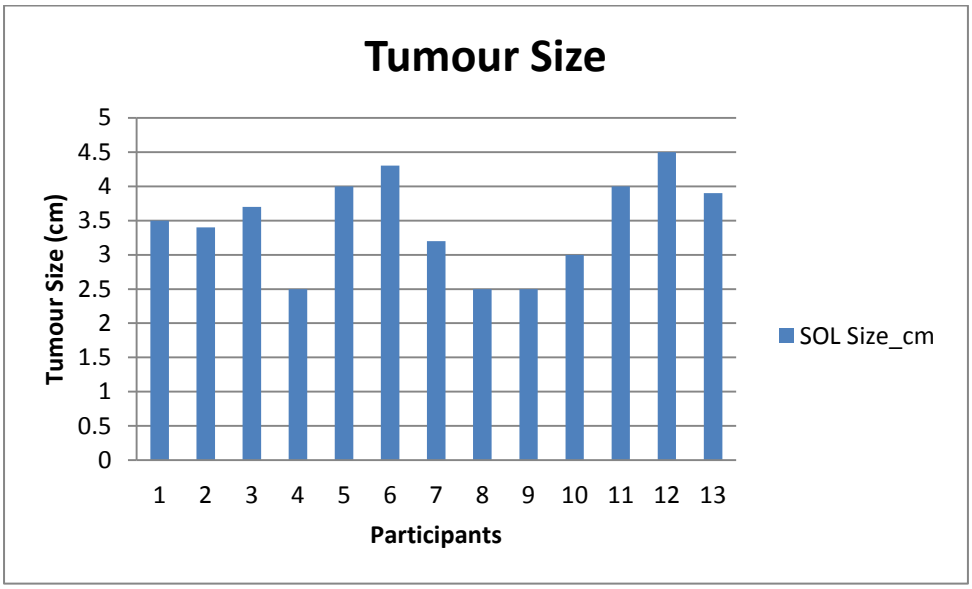


Figure 5b Bar graph of participant tumour size

Eleven of the tumours were intra-axial and two were extra-axial. The histological classification of the tumours were metastatic carcinoma in seven patients (53.9%), one ependymoma (7.7%), one atypical choroid plexus papilloma (ACPP) (7.7%), two meningiomas (15.4%), one haemangioblastoma (7.7%) and one pilocytic astrocytoma (7.7%). According to the WHO classification of brain tumours, four tumours were grade one, two grade two tumours and seven grade four tumours. No tumour had a grade three WHO classification. Six of the tumours were of primary origin with seven tumours of secondary origin. Of the seven metastatic tumours, three had the primary location in the lung, two in the breast and one in each the colon and the ovaries. Seven participants required radiotherapy post surgery while six participants did not. Four participants required post-operative chemotherapy. All participants had an MRI scan pre surgery and twelve participants had a CT scan. The tumour data of the study participants are summarized in table 5d (overleaf).

Table 5d Tumour parameters of participants

Variable	Subjects (n= 13) %
Size of Tumour (cm) Mean and SD	3.5 ± 0.7
Location of Tumour	4^{th} Ventricle = 3 (23.1%)
	Cerebellar Vermis = 2 (15.4%)
	Cerebellar Hemisphere = 8 (61.5%)
Intra/extra axial tumour	Intra-axial = 11 (84.6%)
	Extra-axial = 2 (15.4%)
Histology of Tumour	Metastatic lesion = 7 (53.9%)
	Ependymoma = 1 (7.7%)
	ACPP = 1 (7.7%)
	Meningioma = 2 (15.4%)
	Haemangioblastoma = 1 (7.7%)
	Pilocytic astrocytoma = 1 (7.7%)
WHO Classification of Tumour	WHO Grade 1 = 4 (30.8%)
	WHO Grade 2 = 2 (15.4%)
	WHO Grade 3 = 0 (0%)
	WHO Grade 4 = 7 (53.9%)
Primary Tumour (n) %	6 (46.1%)
Secondary Tumour (n) %	7 (53.9%)
Requiring Post-op Radiotherapy	Yes = 7 (53.9%)
	No = 6 (46.1%)
Requiring Post-op Chemotherapy	Yes = 4 (30.8%)
	No = 9 (69.2%)

5.7 Surgical parameters of participants at baseline

Eleven participants underwent a craniectomy procedure and two participants had craniotomies to expose the tumour. Nine participants had a total excision of the tumour while four had a sub-total excision. Nine participants required only one surgical procedure, two participants required two, one participant required three procedures and one participant required five surgeries. Two participants had the presence of midline shift on MRI scan and seven participants had mass effect on MRI scan. Eight participants had the presence of hydrocephalus on MRI scan. One individual required the insertion of a shunt and four participants required EVD insertion. Four participants developed post-operative haemorrhages. Four participants required admission to the intensive care unit post surgery. The intervention data of the study participants are summarized in table 5e (overleaf).

Table 5e Participant interventions

Variable	Subjects (n=13) %	
Exposure Technique	Craniectomy = 11 (84.6%)	
	Craniotomy = 2 (15. 4%)	
Number of Surgical Interventions	One surgery = 9 (69.2%)	
	Two surgeries = 2 (15.4%)	
	Three surgeries = 1 (7.7%)	
	Four surgeries = 0 (0%)	
	Five surgeries = 1 (7.7%)	
Total Excision	Yes = 9 (69.2%)	No = 4 (30.8%)
Subtotal Excision	Yes = 4 (30.8%)	No = (69.2%)
Presence of Mass Effect	Yes = 7 (53.9%)	No = 6 (46.1%)
Presence of Midline Shift	Yes = 2 (15.4%)	No = 11 (84.6%)
Presence of Hydrocephalus	Yes = 8 (61.5%)	No = 5 (38.5%)
Requiring Shunt Insertion	Yes = 1 (7.7%)	No = 12 (92.3%)
Requiring EVD Insertion	Yes = 4 (30.8%)	No = 9 (69.2%)
Post-operative Haemorrhage	Yes = 4 (30.8%)	No = 9 (69.2%)
Post-operative ITU admission	Yes = 4 (30.8%)	No = 9 (69.2%)

5.8 Presenting Features

Participants in the study reported several pre-surgical features of the tumour. Nine participants complained of headache on admission. Seven participants had nausea and five reported vomiting pre admission. Five participants had visual disturbances. Seven participants experienced dizziness. Two participants complained of vertigo. One participant had tinnitus. No participant experienced oscillopsia. All participants were GCS intact and all scored 15/15 at admission. At admission twelve participants were independently mobile with one participant using a zimmer frame. The presenting features of the study participants are summarized in table 5f (below).

Table 5f Presenting features of participants

Variable	Subjects (n = 13) %	
Headache	Yes: 9 (69.2%)	No: 4 (30.8%)
Nausea	Yes: 7 (53.9%)	No: 6 (46.2%)
Vomiting	Yes: 5 (38.5%)	No: 8 (61.5%)
Visual Disturbance	Yes: 5 (38.5%)	No: 8 (61.5%)
Dizziness	Yes: 7 (53.9%)	No: 6 (46.2%)
Vertigo	Yes: 2 (15.4%)	No: 11 (84.6%)
Tinnitus	Yes: 1 (7.7%)	No: 12 (92.3%)
Oscillopsia	Yes: 0 (0%)	No: 13 (100%)
Mobility Status	Independent: 12 (92.3%)	
	Zimmer frame: 1 (7.7%)	
GCS on Admission	15/15: 13 (100%)	

5.9 Assessments

This section catalogues the testing battery completed for each participant.

5.9.1 Balance

Outcome measure: Equitest (Computerized dynamic posturography)

Computerized dynamic posturography (Equitest) testing was carried out with participants at three different stages during the course of the study and was the primary outcome measure of the study. The sensory organization test (SOT) was the test protocol utilised. Initial testing was prior to the participant undergoing a surgical intervention (T1), second testing was post-operatively while the participant was an inpatient in the hospital (T2) and finally when the participant returned to the hospital for their clinic review at six weeks (T3). At T1, all thirteen participants had the testing completed. A mean composite score of 58.7 ± 16.2 was achieved with the minimum being 34 and the maximum 83.

At T2 nine participants had the testing completed. A mean composite score of 61.3 ± 11.0 was achieved at this point with the minimum result 49 and the maximum 86. Participants failed to engage in T2 Equitest data collection due to admission to ITU (n=2; 15.4%), discharge home prior to testing completion (n=1; 7.7%) and excessive pain levels limiting engagement (n=1; 7.7%).

At T3 eight participants had the testing completed. A mean composite score of 68.1 ± 18.8 was achieved with a minimum composite score of 29 and maximum score of 85. Participants failed to engage in T3 Equitest data collection due to follow-up care transferred to local services in Galway (n=1; 7.7%), inability to complete assessment due to post-operative morbidity (n=2; 15.4%) and on-going adjuvant therapy (radiation and chemotherapy) limiting participation (n=2, 15.4%). The SOT data for the three tested time-points is presented in table 5g (overleaf).

Table 5g SOT composite equilibrium data

Time-point	Composite Score (Mean and SD)
One (Pre-operative) (n=13)	58.7 ± 16.2
Two (Post-operative) (n=9)	61.3 ± 11.0
Three (Clinic Review – 6 weeks) (n=8)	68.1 ± 18.8

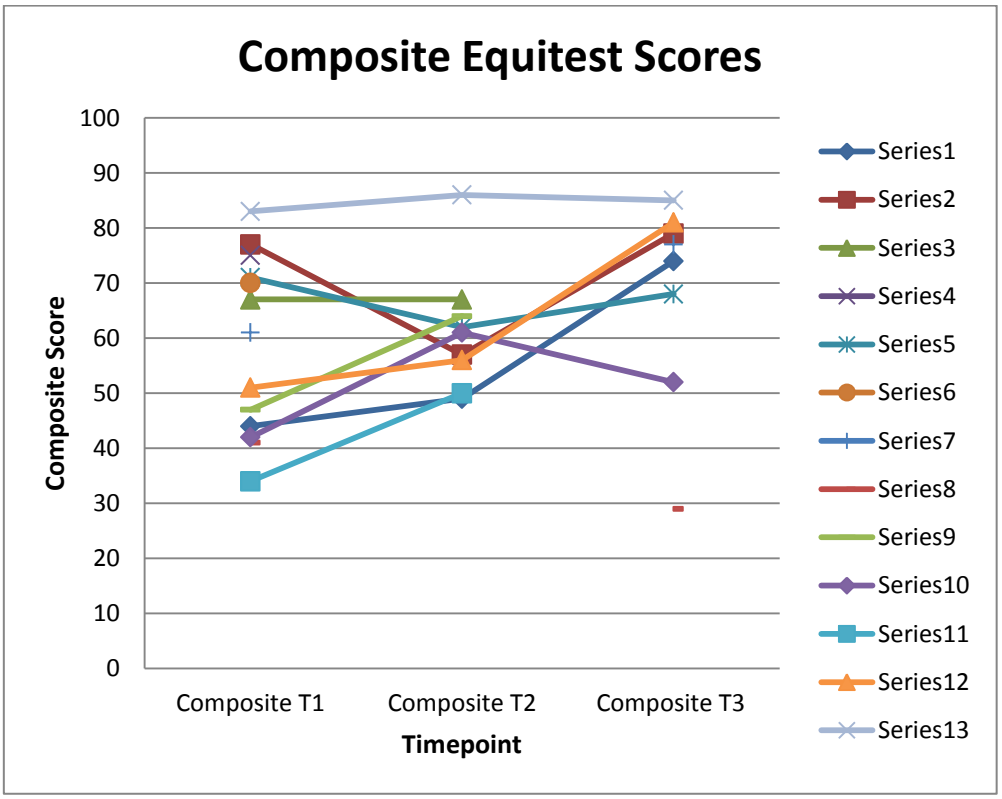


Figure 5c All available SOT composite scores over T1, T2 and T3 for all participants

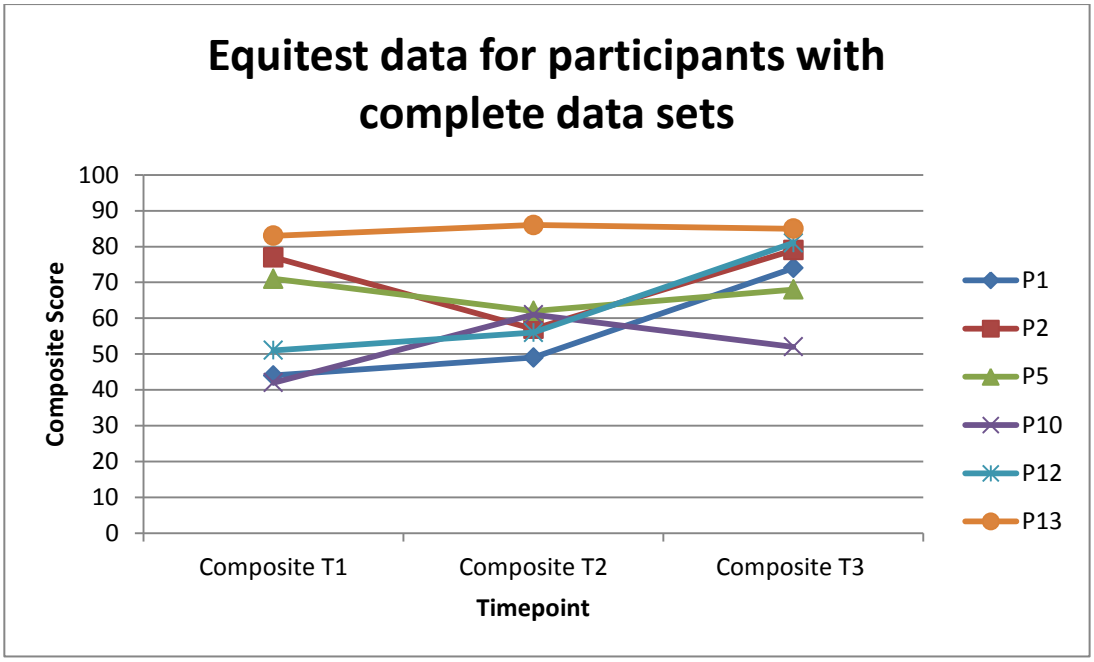


Figure 5d SOT composite data for participants with complete data sets at all time-points

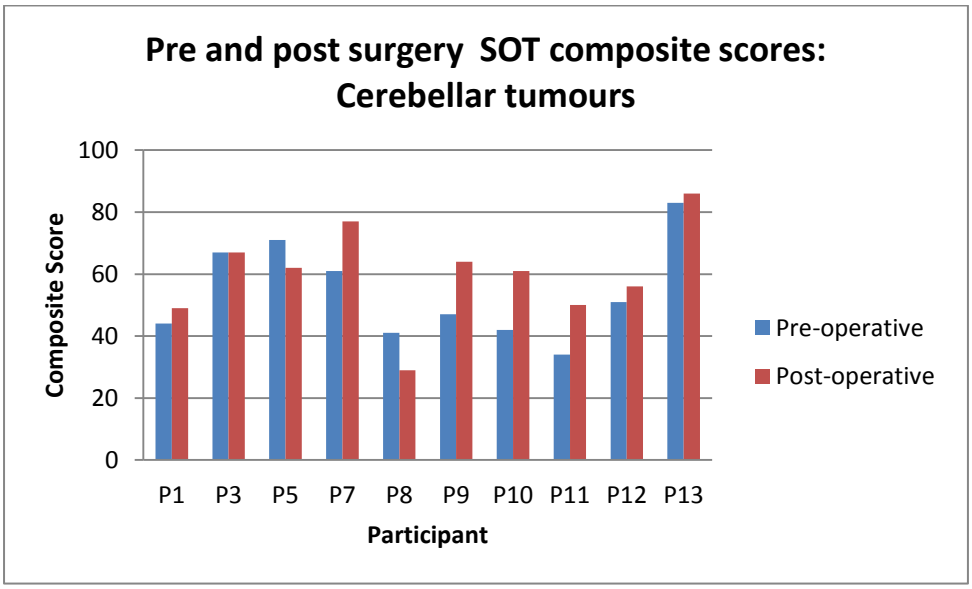


Figure 5e Pre and post-operative Composite SOT scores for participants with cerebellar tumours

5.9.2 Equitest: Condition Five and Six of the Sensory Organisation Test (SOT)

Conditions five and six of the SOT challenge a person's ability to use input from the vestibular system. The mean and standard deviation for condition five and six was calculated for each time-point. Table 5h below outlines the data from the two test conditions. The average number of falls experienced by the participants during testing of conditions five and six is also represented.

Table 5h Condition five and six of the SOT

SOT condition	Mean and SD	Number of Falls
Condition Five		
T1 (n=13)	25.8 ± 27.6	1.6
T2 (n=9)	20 ± 18.7	1.5
T3 (n=8)	44.5 ± 30.2	0.9
Condition Six		
T1 (n=13)	35.7 ± 26.9	1.2
T2 (n=9)	39.3 ± 30.2	1.1
T3 (n=8)	45.0 ± 31.6	1.0

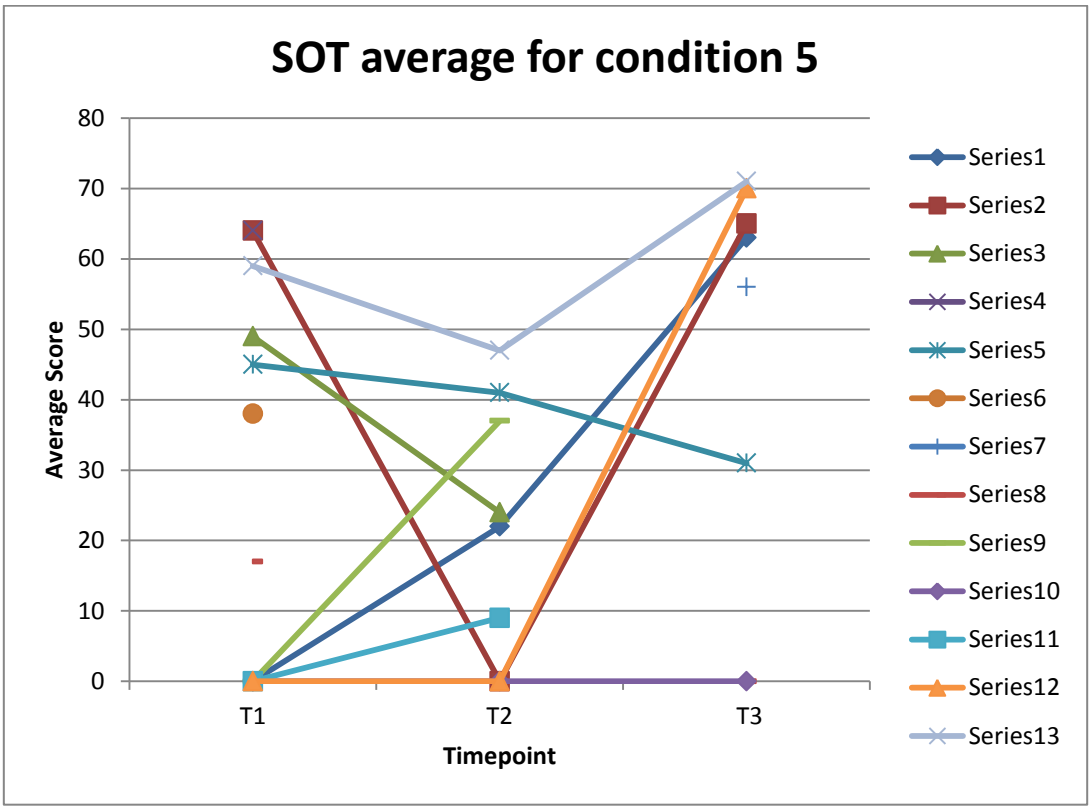


Figure 5f Average equilibrium scores for each participant on condition 5 of the SOT

Foot note: Reasons for missing data: P3 (T3) follow-up care transferred to another site, P4(T2, T3) Assessments limited by post-operative morbidity, P6(T2, T3) Assessments limited by post-operative morbidity, P7 (T2) Discharge from hospital prior to testing completion, P8 (T2) Refusal to participate due to post-operative pain, P9 (T3) On-going adjuvant therapy (radiation and chemotherapy) limiting participation, P11(T3) On-going adjuvant therapy (radiation and chemotherapy) limiting participation.

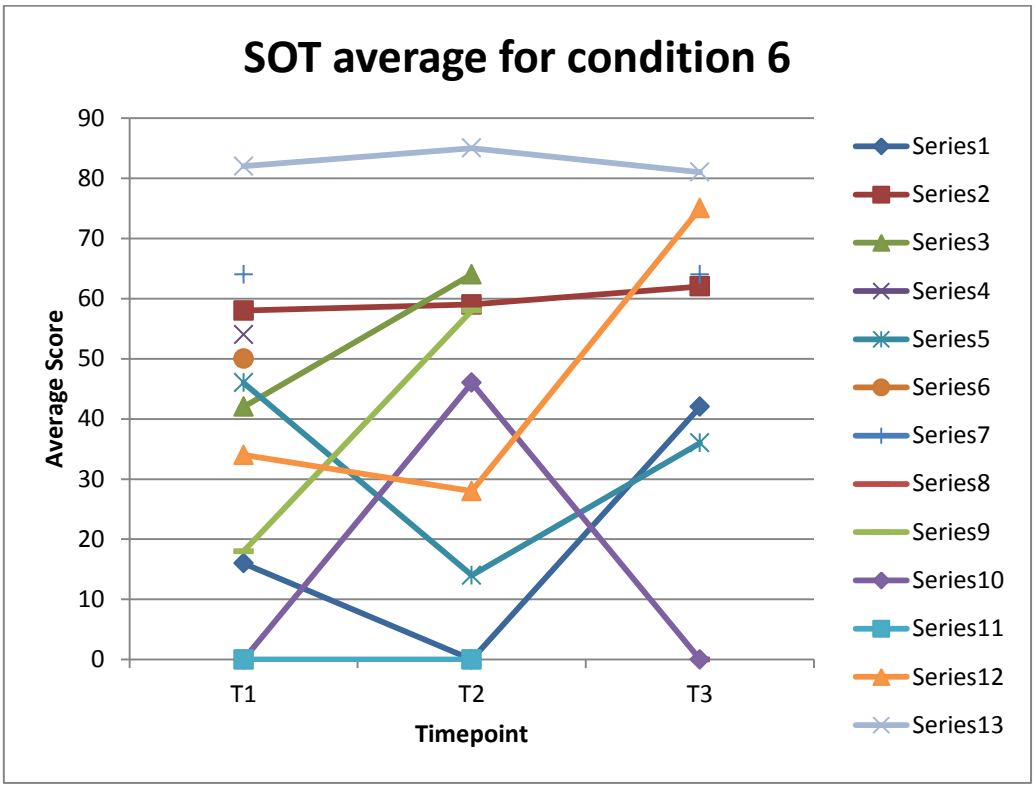


Figure 5g Average equilibrium scores for each participant on condition 6 of the SOT

Foot note: Reasons for missing data: P3 (T3) follow-up care transferred to another site, P4(T2, T3) Assessments limited by post-operative morbidity, P6(T2, T3) Assessments limited by post-operative morbidity, P7 (T2) Discharge from hospital prior to testing completion, P8 (T2) Refusal to participate due to post-operative pain, P9 (T3) On-going adjuvant therapy (radiation and chemotherapy) limiting participation, P11(T3) On-going adjuvant therapy (radiation and chemotherapy) limiting participation.

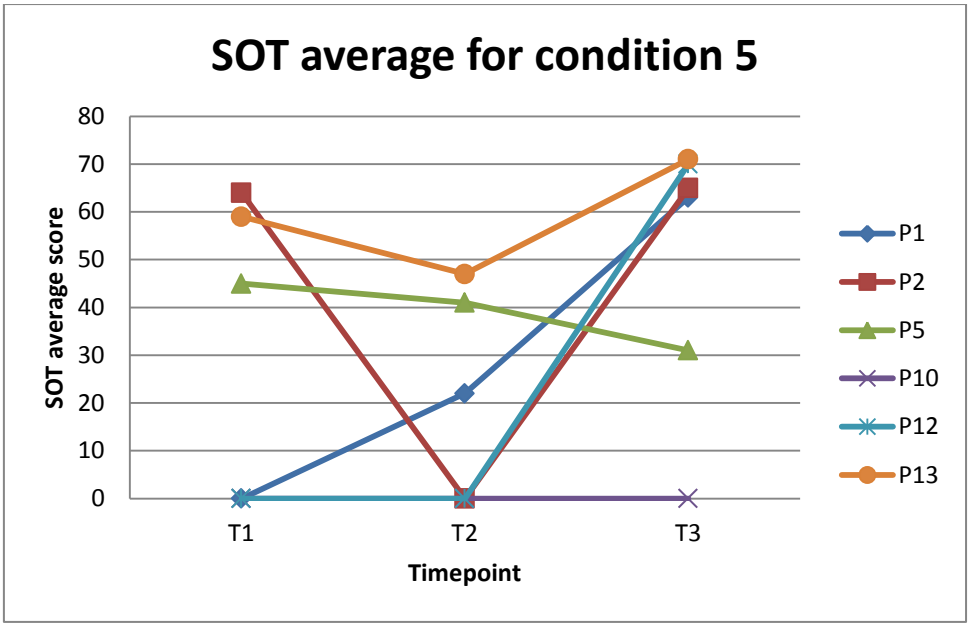


Figure 5h Average equilibrium scores for participants with complete datasets on condition 5 of the SOT

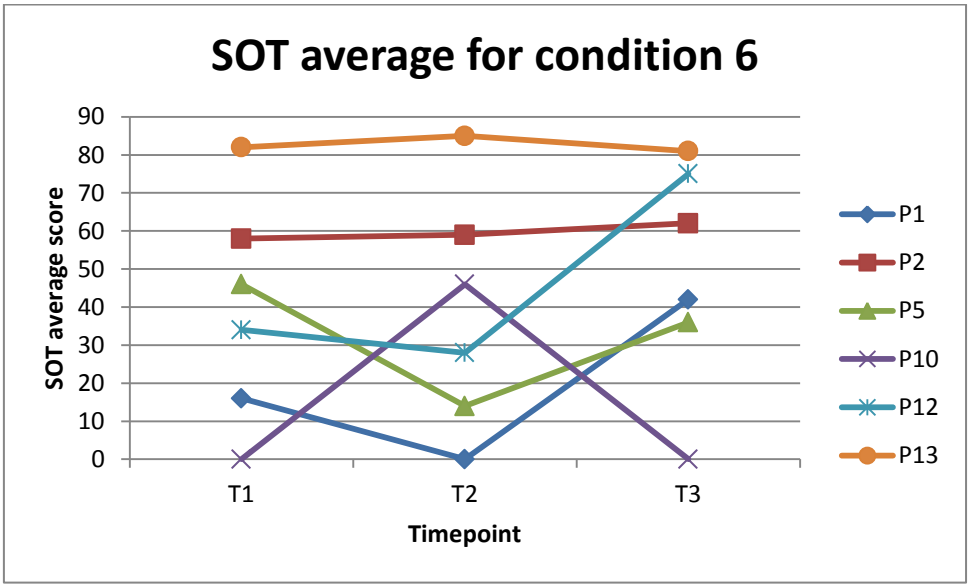


Figure 5i Average equilibrium scores for participants with complete datasets on condition 6 of the SOT

5.9.3 Gait

Outcome measure: 10 metre walking tests at preferred and max gait speeds and with horizontal head turns.

Walking speed was assessed using 10m walking tests. The walking tests were completed under three different conditions; self selected walking speed, maximum speed and self selected walking speed with included horizontal head turns. An average of the results of three trials was included for each participant, for analysis.

At T1 all thirteen participants completed the testing, at T2 nine participants completed testing and at T3 eight participants completed the testing. The preferred gait speed data for the three tested time-points is presented in table 5i (below).

Table 5i Preferred self-selected gait speed

Time-point	Mean and SD (m/s)
T1 (n=13)	1.3 ± 0.3
T2 (n=9)	0.9 ± 0.4
T3 (n=8)	1.3 ± 0.2

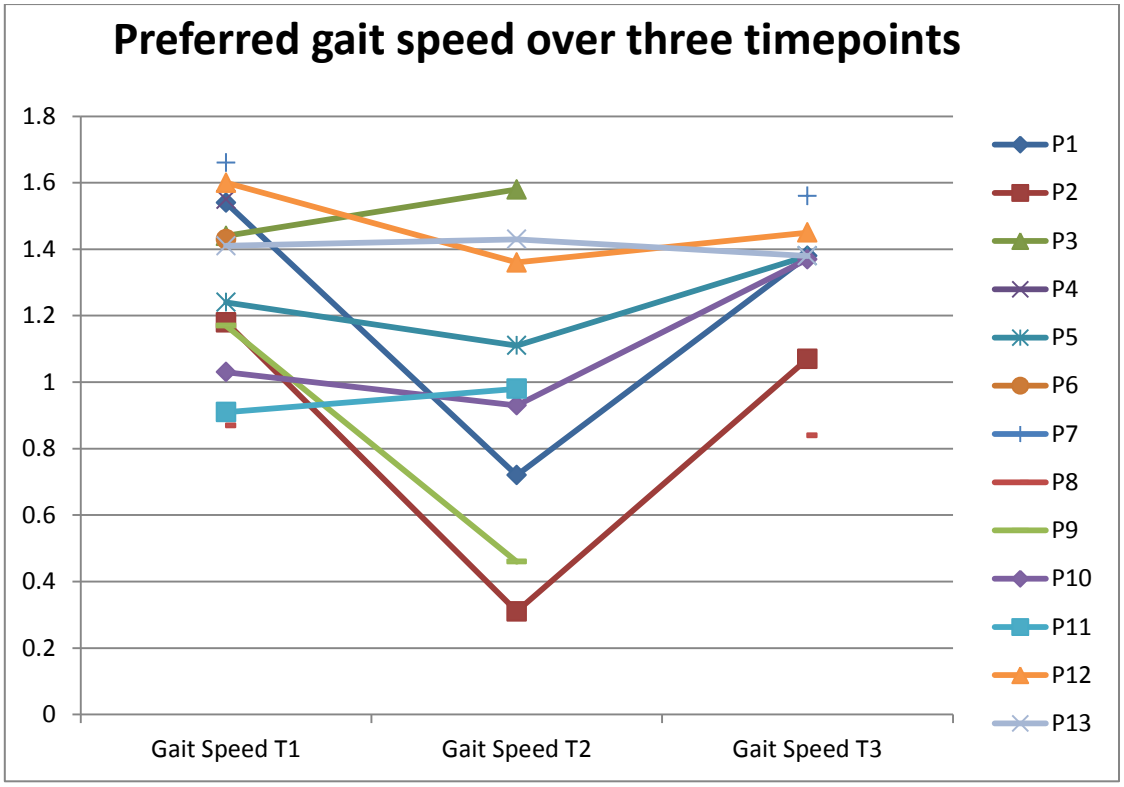


Figure 5.9.3.1 Graphical representation of preferred gait speed for all participants at all three time-points

At T1 all thirteen participants completed the testing, at T2 nine participants completed testing and at T3 eight participants completed the testing. The maximum gait speed data for the three tested time-points is presented in table 5j (below).

Table 5j Maximum Gait Speed

Time point	Mean and SD (m/s)
T1 (n=13)	1.7 ± 0.4
T2 (n=9)	1.2 ±0 .4
T3 (n=8)	1.5 ± 0.3

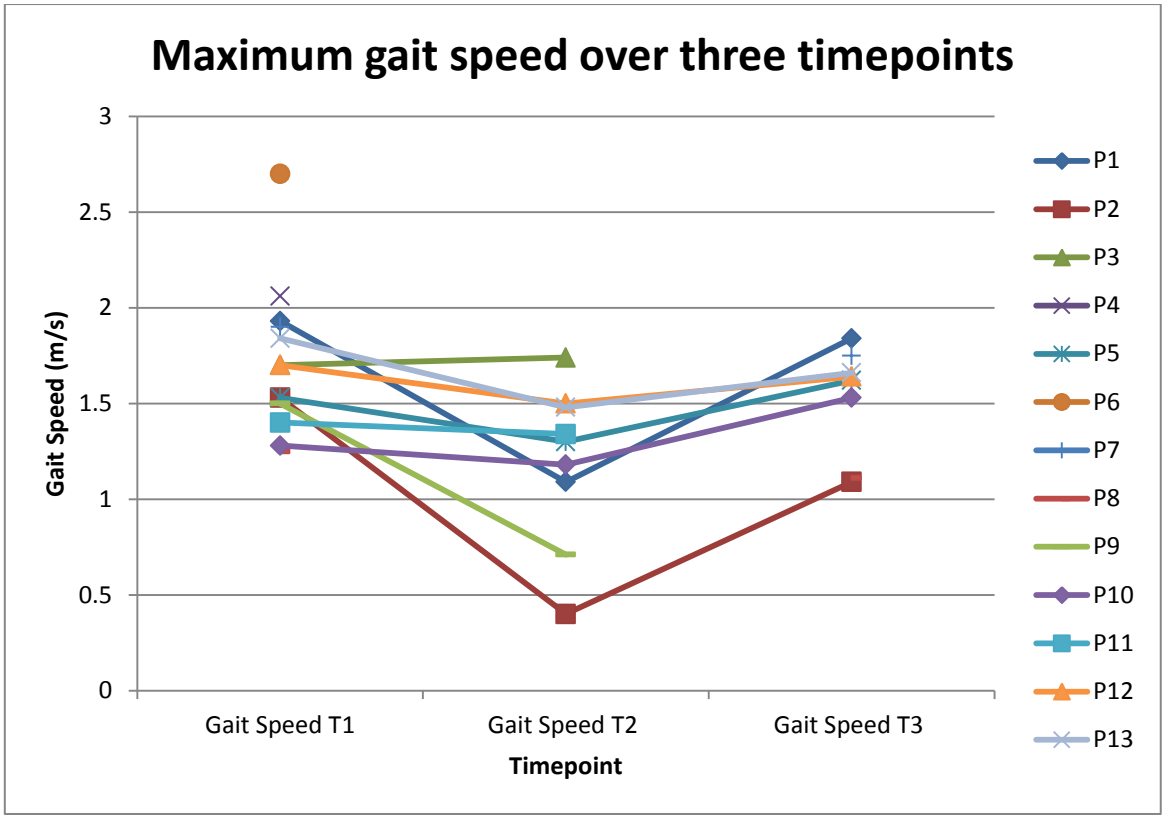


Figure 5k Graphical representation of maximum gait speed for all participants for all three time-points

At T1 all thirteen participants completed the testing, at T2 nine participants completed testing and at T3 eight participants completed the testing. Mean preferred walking speed with associated horizontal head turns is outlined in table 5k (below).

Table 5k Gait speed with horizontal head turns

Time-point	Mean and SD (m/s)
T1	1.3 ± 0.3
T2	0.9 ± 0.4
T3	1.1 ± 0.5

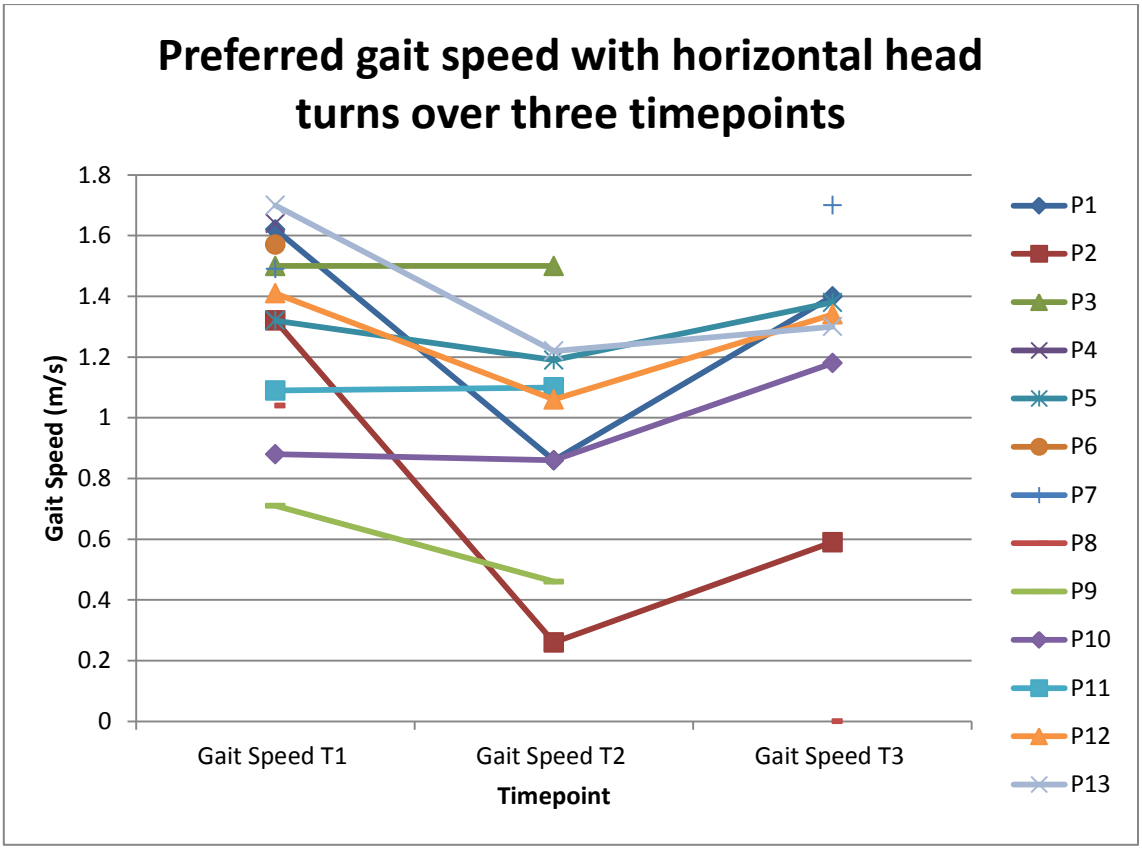


Figure 5l Graphical representation of preferred gait speed with associated horizontal head turns for all three time-points

5.9.4 Upper Limb Dexterity

Outcome measure: Nine Hole Peg Test (NHPT)

Upper limb dexterity was measured using the NHPT and was completed for bilateral upper limbs. Eleven participants (85%) were right hand dominant and two participants were left hand dominant (15%). Completion of the NHPT for both upper limbs was carried out at T1, T2 and T3 for participants. Pre-operatively at T1 the average speed of completion of the test was 24.34 seconds, at T2 average speed was 23.35 seconds and at T3 average speed was 24.30 seconds for the right upper limb. For the left upper limb at T1 the average speed of completion was 28.24 seconds, at T2 average speed was 25.46 seconds and at T3 average speed was 25.90 seconds. All thirteen participants completed the NHPT at T1, nine completed testing at T2 and eight participants completed testing at T3.

Table 5l Right Upper Limb Dexterity

Time point	Mean and SD (secs)
T1	24.3 ± 13.7
T2	23.4 ± 4.2
T3	24.3 ± 14.5

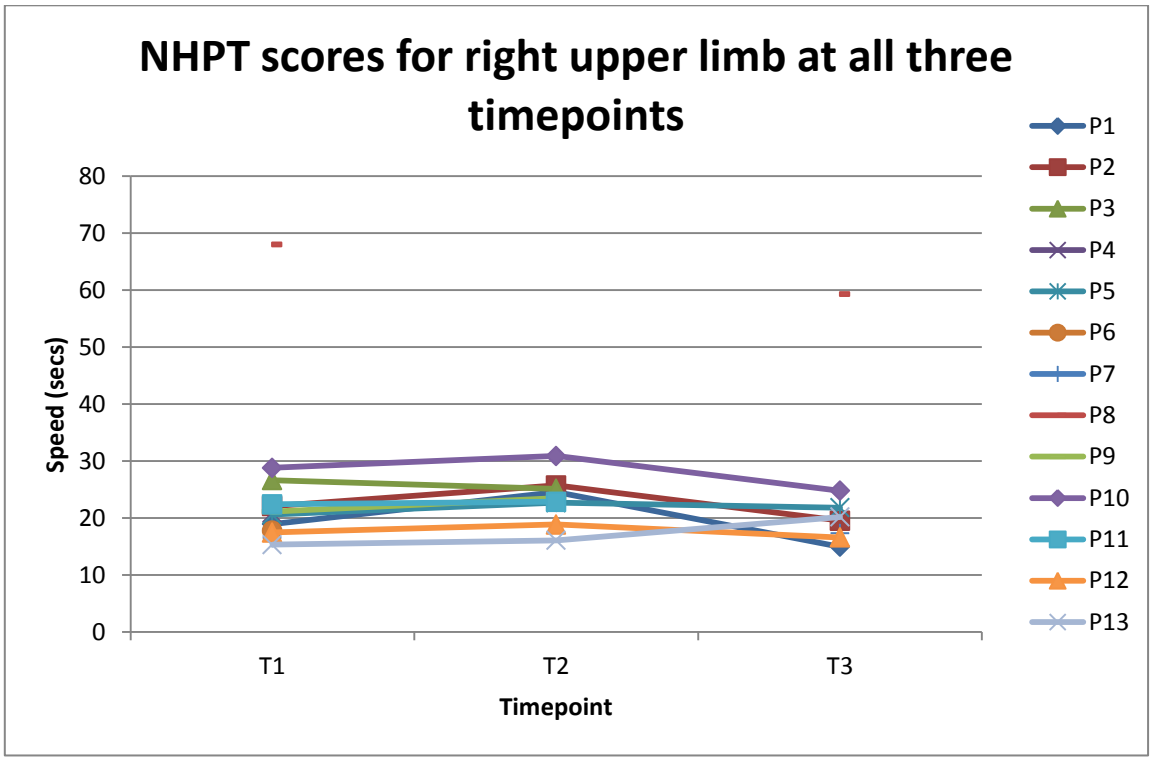


Figure 5m Right upper limb NHPT score in seconds for each participant at all three time-points

Table 5m Left Upper Limb Dexterity

Time point	Mean and SD (secs)
T1	28.2 ± 21.0
T2	25.5 ± 5.6
T3	25.9 ± 12.3

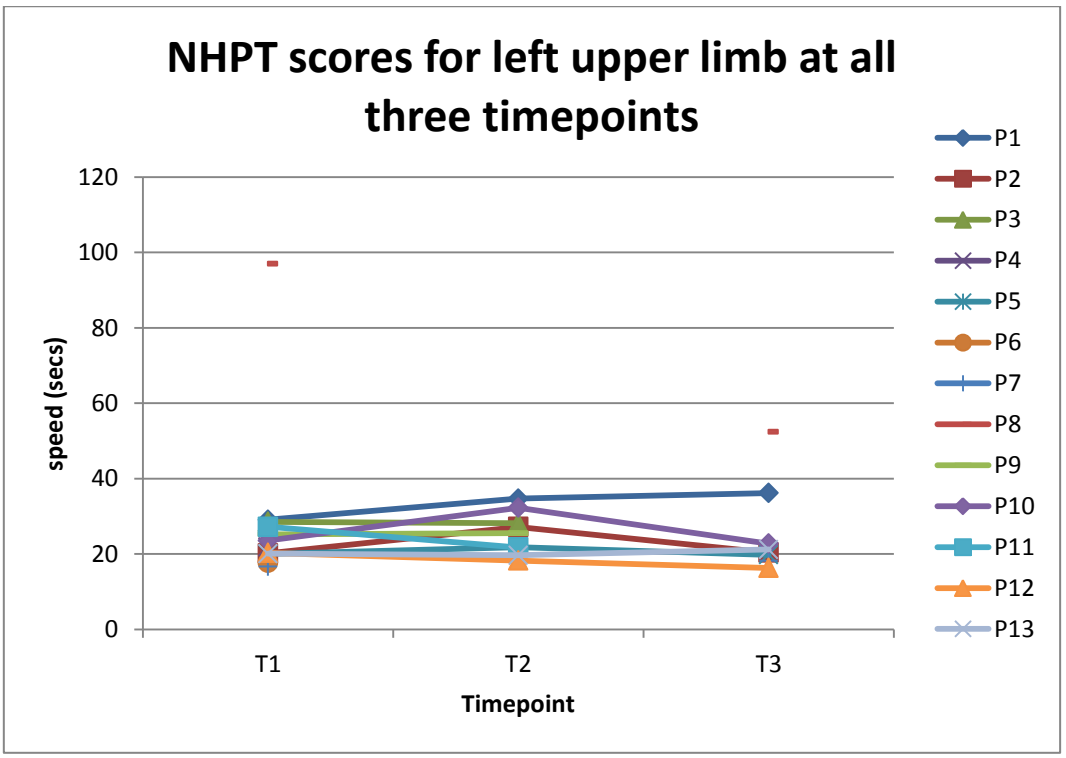


Figure 5n Left upper limb NHPT score in seconds for each participant at all three time-points

Ten participants (77%) were diagnosed with a tumour of the cerebellum. Eight participants (62%) had an intramedullary lesion of the cerebellum and two had an extra-medullary lesion (15%). Eight of the participants had the tumour occur within the cerebellar hemispheres and two occurred within the vermis. The mean age of the participants with tumours of the cerebellum was 54 ± 13.35 years. Figure 5o represents the mean completion times of the NHPT for all participants with a cerebellar tumour. Data for the right upper limb is represented.

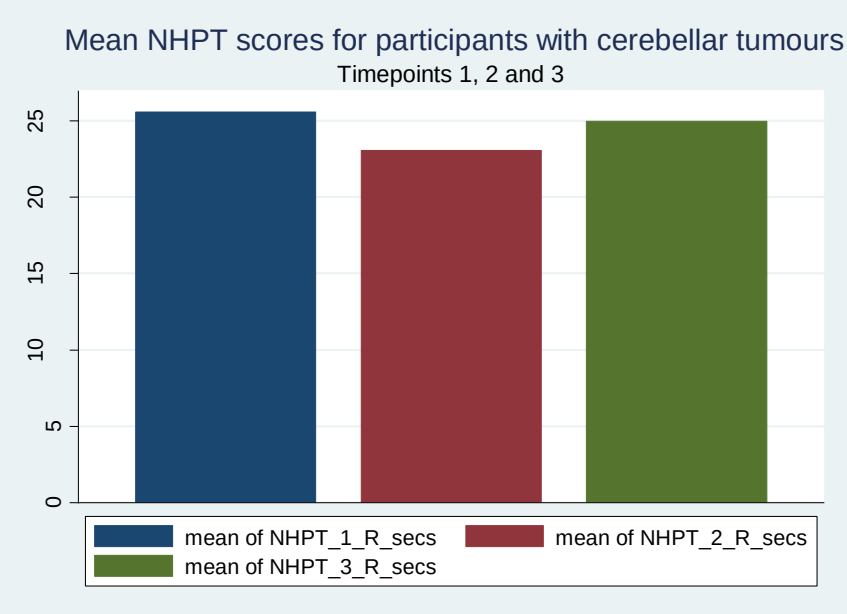


Figure 5o Mean NHPT completion times at T1, T2 and T3 for participants with cerebellar tumours (n=10)

5.9.5 Dizziness

Outcome measure: Dizziness handicap inventory

Dizziness of the participants was captured by using the Dizziness Handicap Inventory, a measure of self-perceived dizziness. This measure was completed at all four time-points in the study. At T1, pre-operatively all thirteen participants completed the DHI, at T2 nine participants completed the DHI, at T3 eight participants completed the DHI and at T4 seven completed the DHI.

Table 5n Dizziness handicap inventory

Time point	Mean and SD
T1 (n= 13)	21.2 ± 22.9
T2 (n= 9)	32.2 ± 30.1
T3 (n= 8)	24.3 ± 28.9
T4 (n= 7)	25.1 ± 26.6

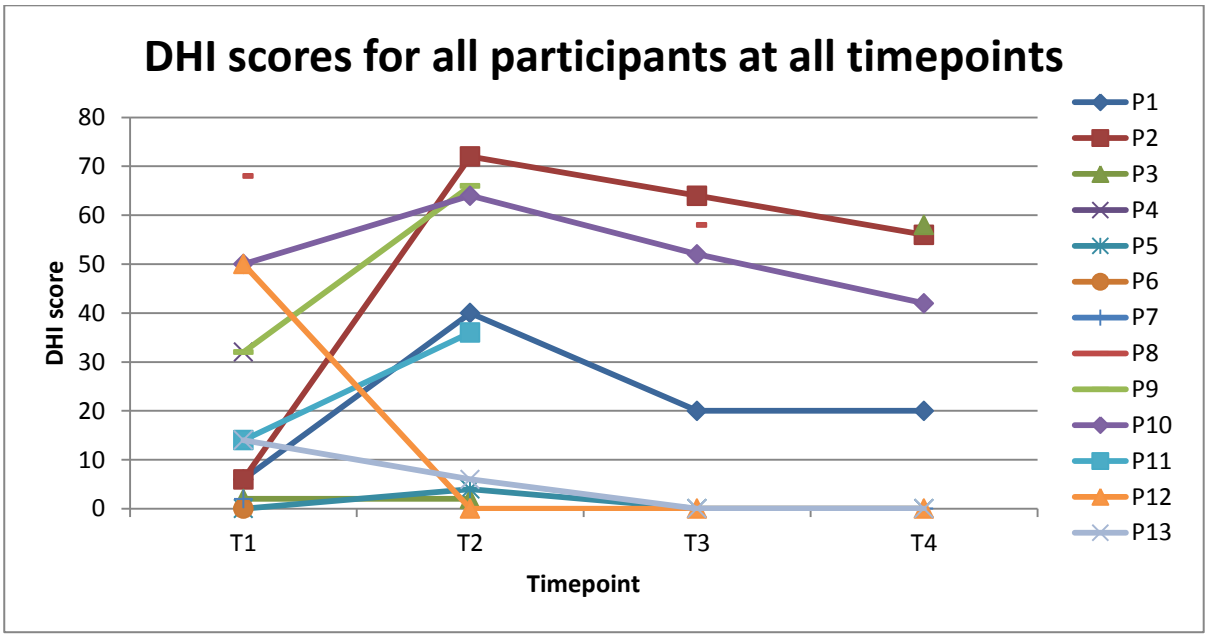


Figure 5p DHI scores for all participants at all time-points

5.9.6 Post-operative pain

Outcome Measure: Box scale for pain

The Box scale for pain was used to capture a subjective measure of the participant's post-operative pain. This measure was completed at T2, T3 and T4 to capture post-operative pain that may impact on ability to participate with physical outcome measures. At T2, 10 participants completed the box scale for pain, eight participants completed the box scale at T3 and eight at T4. One participant refused to engage in T2 testing due to reported significant post-operative pain.

Table 5o Box Scale for Pain

Time point	Mean and SD
T2 (n=10)	3.1 ± 2.6
T3 (n=8)	0.3 ± 0.7
T4 (n=8)	0.5 ± 1.1

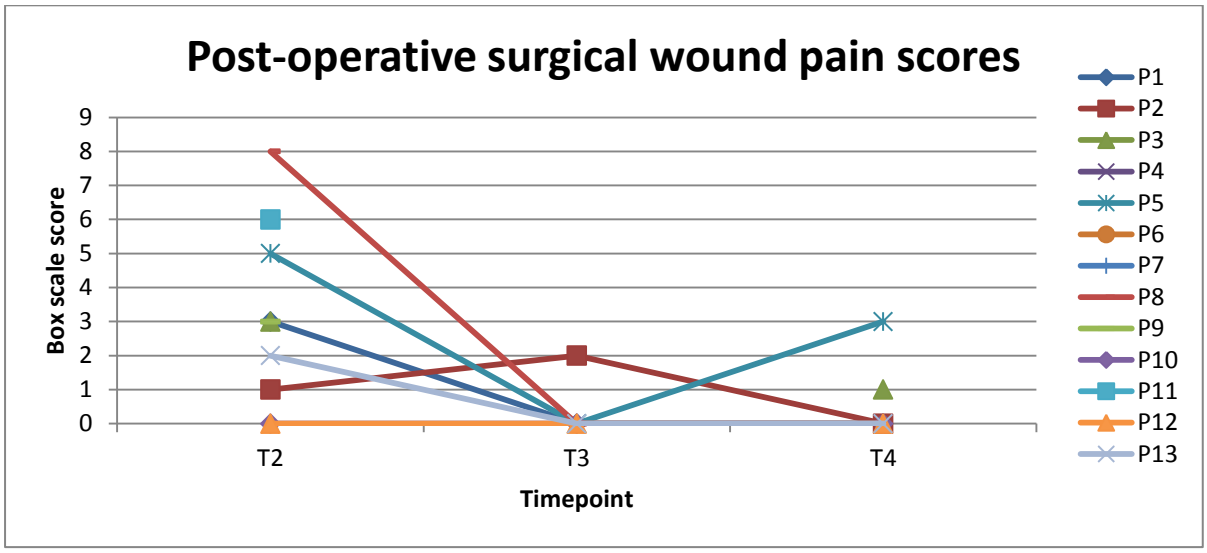


Figure 5q Post-operative surgical site wound pain as captured on the Box scale for pain

Footnote: Rating scale for pain ranging from zero to ten

5.9.7 Quality of Life

Outcome Measure: Linear Analogue Scale Assessment

The LASA scale was completed for measurement of the participant's perception of quality of life in five different domains. They included overall quality of life, intellectual wellbeing, physical wellbeing, emotional wellbeing and spiritual wellbeing. Twelve participants completed the measures at T1 and eight completed the T4 measures. The LASA values for pre-operative testing are outlined in table 5p (below).

Table 5p LASA scores at T1 and T4

Quality of Life Variables	Mean and SD	
	T1	T4
Overall quality of life	7.3 ± 2.5	7.1 ± 2.2
Intellectual well-being	7.6 ± 2.1	7.9 ± 2.0
Physical well-being	7.9 ± 2.4	6.9 ± 2.5
Emotional well-being	7.3 ± 1.6	7.3 ± 1.4
Spiritual well-being	8.3 ± 2.4	8.3 ± 1.6

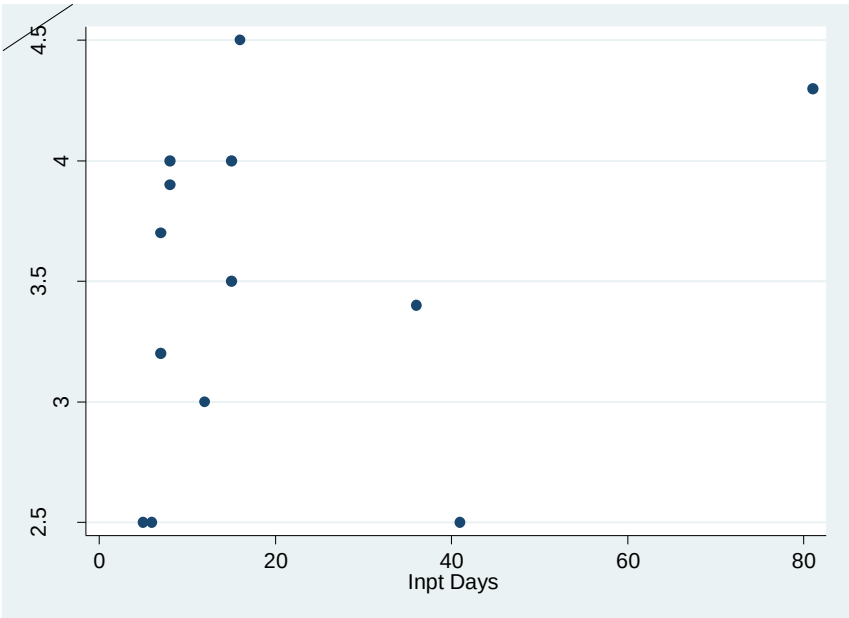
5.10 Inpatient Days

The number of days each participant was an inpatient in Beaumont Hospital was captured. The mean number of days in hospital was 19.8, with the minimum number of days five and the maximum number of days 81.

Table 5q Inpatient Days

	Mean and SD
Inpatient Days (n=13)	19.8 ± 21.6

Figure 5r (below) is a graphical representation of the correlation between the size of a participant's tumour and the association with number of inpatient days in Beaumont Hospital. A non-linear relationship between the size of the tumour and the number of inpatient days is depicted.



Chapter 6: Discussion

6.1 Introduction

The primary aim of this research study was to characterise balance, gait, dizziness, upper limb dexterity and quality of life in patients, pre and post posterior fossa tumour surgery. The secondary aim was to evaluate the demographic and tumour characteristics of the included participants. The experimental hypothesis was that subjects with posterior fossa tumours would demonstrate reduced balance, reduced gait speed, increased dizziness and reduced upper limb dexterity and quality of life post-operatively when compared with their pre-operative status. The results of the research study showed a small increase in the primary endpoint, composite equilibrium score on the SOT of computerized dynamic posturography post-operatively, which does not support the study hypothesis. A reduction in gait speed for all testing conditions, a reduction in nine hole peg test completion speed and an increase in post-operative dizziness were also identified, supporting the study hypothesis in relation to secondary endpoints.

6.2 Description of the study group

The cohort of recruited participants in this research study consisted of eight females and five males, who demonstrated a similarity in the inter-gender age profiles. The majority of research currently available in relation to posterior fossa tumours has contained paediatric cohorts. The propensity for investigation of this topic in children relates to the high occurrence rate of paediatric posterior fossa tumours (Zakrzewski et al., 2003), high risk of malignancy (Park et al., 1983) and the associated morbidity (Cochrane et al., 1994). The limited research currently available in the adult population, profiling the impact of surgery and the resultant impairments, makes this a novel piece of neuro-oncology research in the adult population.

This research study classified an adult as an individual over the age of 18 years and only adult participants were recruited for inclusion and participation. Within the catalogue of adult research, discrepancies exist in relation to the classification age of adults. In a profile of medullablastoma patients, a common posterior fossa tumour diagnosis, those over the age of fourteen were classified as adults (Kumar et al., 2015), while Menon et al (2008) classified an adult as being over the age of 16. A large volume of literature is available that

classifies participants as those over the age of 18 (Greenberg et al., 2001) but care must be taken when making comparisons between the research populations given the discrepancies that exist between presentation, management, histology and prognosis of this complex population, based on age.

6.3 Presenting Features

A large variety of presenting features were evident in the study cohort. Headache historically has been classified as one of the most frequently occurring features of a brain tumour (Buckner et al., 2007) and was present in nine of the study participants (69.2%), at first presentation to a medical facility. According to the international classification of headache disorders (2013), brain tumour related headache has a tendency to present worst in the morning, be aggravated by coughing and be progressive in nature. In a study investigating the characteristics of headaches in brain tumour patients, Schankin et al (2007) found headaches to be a presenting feature in 60% of their participants, with only one study participant (2%), experiencing headache as their sole feature at presentation. Seventy-one per cent of the participants diagnosed with an infra-tentorial tumour experienced headache, which is similar to the occurrence rate of tumour related headache in this study. In a study reviewing the presenting characteristics of patients with posterior fossa haemangioblastomas, 64% presented with head pain classified as being related to changes in intracranial pressure or more localised occipital pain (Jeffreys, 1975). Jeffreys (1975) included the data of five spinal haemangioblastoma patients in their study, which may account for the slightly lower occurrence of headache, as spinal pathology would not be routinely associated with the presence of headache. The low incidence of independently occurring headache highlights the importance of careful evaluation of patients, to ensure associated features are recognised to assist in the diagnosis of those at risk of a sinister diagnosis.

Brain tumour histology can influence the potential of experiencing tumour related headache. In this study, cerebellar metastases (METS) was the most frequently occurring histology type, with 71% of those diagnosed with a metastatic tumour in the cerebellum experiencing headaches (n = 7; 54%). Schankin et al (2007) did not identify any clinical significance between the diagnosis of a metastatic lesion and the increased incidence of headache but they did find diagnosis of a meningioma was associated with a trend towards

increased presence of headache (P = 0.06). Only two individuals (14.7%) in this study were diagnosed with a meningioma and both had headache as a presenting feature. Comparison of presenting features between the two study cohorts is difficult as Schankin et al (2007) did not restrict inclusion, based on cerebral location of the tumour. This study included only individuals with a tumour in the posterior fossa and as a result a trend cannot be formulated, based on the small cohort numbers and variations in presentation. In a profile of 109 patients with cerebellar metastases, 38% experienced severe headache attributed to consequences of raised intracranial pressure secondary to hydrocephalus (Yoshida and Takahashi, 2009). A similar incidence was noted by Lassman and DeAngelis (2003) who found headache in 31% of a cohort of 1,013 patients diagnosed with cerebral metastatic lesions. The discrepancy between the higher rate of headache associated with the presence of a cerebellar metastases in this study, may be attributed to the overall small sample size and the limited number of cerebellar metastases diagnosis, on which to formulate conclusions.

In individuals diagnosed with a brain tumour, presenting features tend to occur in clusters, with independent presenting features being rare. These features are often the consequence of raised intracranial pressure and are considered a common side-effect of a tumour of the posterior fossa. In the posterior fossa, headache associated with elevated intracranial pressure often presents with vomiting. In this study, four participants (31%) presented with both headache and vomiting on initial medical review, while three participants (21%) showed no signs of headache or vomiting as part of their presenting features. The presence of a vomiting centre has been catalogued in the “area postrema in the floor of the caudal part of the fourth ventricle” (Baker and Bernat, 1985). Tumours occurring in this region of the brain have been shown to impair appetite and cause nausea (Abecassis et al., 2013). Projectile patterns of vomiting have also been linked to involvement of the pons and the cerebellar peduncles (Baker and Bernat, 1985). In this study, five participants (38%) had features of headache and vomiting at presentation and four were diagnosed with metastatic lesions, all occurring in the cerebellum and one atypical choroid plexus papilloma of the fourth ventricle. In a profile of 111 patients with brain tumours, researchers found the presence of altered neurological exam, nausea, vomiting or a change in previous headache pattern generally indicative for the presence of a brain tumour (Forsyth & Posner, 2003).

While this study sample remains too small to extrapolate robust conclusions on the correlation of headache and vomiting, in this population it raises the question of a potential correlation that could be further explored, in the future, with a larger patient cohort.

6.4 Tumour Characteristics

A secondary aim of this research study was to investigate the tumour characteristics of the included participants. Within the posterior fossa, metastatic lesions remain the most commonly occurring tumour type in adult populations, with 53% of the participants in this study being diagnosed with metastatic lesions. The profile of metastatic primary tumour location within this study mirrors that of international research (Aragon-Ching and Zujewski, 2007, Nguyen et al., 2009). Lung cancer remains the most frequent, primary tumour that metastasises to the brain and breast cancer represents the second (Gavrilovic and Posner, 2005). In this study three participants were being treated for a secondary metastatic lesion to the cerebellum, resulting from a lung primary (23%) and two with a breast primary (15%). One male participant had a colorectal primary (7.7%) and one female participant an ovarian primary (7.7%). An American study investigating occurrence rates of metastatic lesions as a consequence of diagnosis with a primary tumour in the year 2007, found a 6% future risk rate, for development of a metastatic brain lesion (Davis et al., 2012). Of the population to develop metastatic lesions, 19.9% originated from a lung primary, 5.1% from a breast primary, 2.3% from colorectal primaries and 0.5% from an ovarian primary. In a Swedish population study, similar trends were identified in a retrospective review of oncology data between the years 1987 and 2006 (Smedby et al., 2009). In both sexes, lung primaries were the most frequent site to metastasise to the brain, 44% in males and 33% in females. Breast primaries accounted for 33% of the primaries in females. The Irish neuro-oncology annual report for 2012 (Neuro-oncology annual report, 2012), reviewed metastatic lesion occurrence rates and the associated primary regions. Lung primaries across both sexes, accounted for 38% of lesions and breast primaries 19%. While this study mirrors the overall international trends in primary tumour sites that metastasize to the brain, the small number of participants in the study and variations in histology, prevents the formulation of robust conclusions.

While metastatic lesions were the most commonly occurring tumour histology in this study, other tumour histology types were also diagnosed in the research cohort. Two participants

were diagnosed with cerebellar meningiomas (14.4%). Both meningiomas provided compressive forces onto the cerebellar hemispheres of the involved participants, which caused the associated features that resulted in presentation to the medical facility. Optimum management of meningiomas is total surgical resection but in the posterior fossa access to the lesion can be complicated, due to the proximity to vascular and neurological tissues and the slow growing nature of this tumour type (Jung et al., 2014). In a review of 158 patients admitted to a Korean institution for the management of an infra-tentorial meningioma, Jung et al (2014) highlighted an 81% gross total resection rate in their population. Both participants (14.4%) in this research study had sub-total excisions of their tumours. Failure to excise the tumour in its entirety requires consideration of supplementary treatments such as radiation therapy (Barbaro et al., 1987). Neither of the participants in this study received adjuvant radiation in conjunction with the surgical procedure, even though full resection of the tumour was not achieved.

One participant (7.7%) was diagnosed with an atypical choroid plexus papilloma. Choroid plexus tumours (CPT) are rare, slow growing tumours that arise from the choroid plexus and are mainly of benign histology. They form less than 1% of adult brain tumours with their primary adult location occurring in the fourth ventricle or cerebello-pontine angle (CPA) (Turkoglu et al., 2014). Atypical choroid plexus papilloma (ACPP) is classified as a choroid plexus tumour displaying some characteristics of malignancy (Gopal et al., 2008), but definite classification criteria remain vague. In this research study one participant was diagnosed with an ACPP, WHO tumour classification Grade two (Louis et al., 2007). Given the propensity of this tumour to develop within the ventricular system it is often causative of hydrocephalus (Turkoglu et al., 2014). While this study participant was not diagnosed with pre-operative hydrocephalus, peri-surgical clot formation resulted in hydrocephalus development, leading to two subsequent surgeries to decompress the brain. The patient died 63 days post-surgically and had significant morbidity which limited post-operative testing. The vascular nature of this tumour heightens the risk of haemorrhage associated with surgical excision. In a profile of 26 patients undergoing surgery for the presence of a CPT, a mortality rate of 15% (4/26) was identified (McGirr et al., 1988). However, the deaths within the cohort were in individuals who received surgery prior to 1950, limiting the ability to draw comparison, based on neurosurgical advancement over several decades. A recent

review conducted in the USA, looked at surgical outcomes in a cohort of 24 individuals with ages ranging from six months to 55 years, diagnosed with CPPs (Safaee et al., 2013). This study mirrored findings of more historical series looking at CPPs, with a noted higher age in individuals with infra-tentorial lesions (p=0.002). Two patients (8%) were diagnosed with atypical CPPs, further highlighting the rarity of this tumour type.

One participant (7.7%) was diagnosed with a cerebellar haemangioblastoma. While considered a rare tumour, accounting for 1.5-2% of all CNS tumours, 7-12% occurs within the adult posterior fossa (Resche et al., 1993). The highly vascular nature of this tumour complicates surgical management due to the high risk of bleeding, often requiring embolisation of the lesion prior to excision (Seong Eom et al., 2011). This participant did not require an embolisation prior to excision, which may be due to the cerebellar location of their lesion. Within the literature, the maximum merit of embolisation has been recognised in lesions occurring within the brainstem (Tampieri et al., 1993). The surgical resection of haemangioblastomas is the internationally accepted best management approach and is generally curative in this tumour type (Tomasello and La Torre, 2014). The participant within this study had a gross total resection of their tumour and did not require any follow-up therapy. The participant's peri-operative course was complicated by the development of a pseudomeningocele, secondary to a CSF leak. In a profile of complications associated with posterior fossa surgical techniques, CSF leak was observed in 10% of the participants who underwent a posterior fossa excision secondary to a cerebellar lesion (Dubey et al., 2009). While 11 patients (2%) of the cohort of 500 participants were diagnosed with a cerebellar haemangioblastoma, the authors did not sub-analyse the number of haemangioblastoma patients who developed CSF leak, limiting the ability to calculate the associated risk of CSF leak in haemangioblastoma excision, within the cohort. Given the high association of this tumour type with the diagnosis of VHL syndrome, the participant underwent testing while an inpatient. The testing was negative for VHL, indicating a diagnosis of sporadic haemangioblastoma.

One participant (7.7%) was diagnosed with a pilocytic astrocytoma. Pilocytic astrocytoma (PA) is a WHO grade one tumour, most commonly occurring in the paediatric population, with an incidence in adults of 0.1 cases per 100,000 person-years, in those over the age of 45 years (Johnson et al., 2012). Considered a very rare brain tumour in adults, little evidence

is available in relation to the clinical course of this tumour in the adult population. In a large series of 127 adult PA patients, 50 of the included cohort had their tumour occurring within the posterior fossa, highlighting 39% localisation within the PF (Theeler et al., 2014). The median age profile of the cohort was 30 years, with the majority of participants aged between 18 and 39 years. The participant within this study, diagnosed with a PA was 21 years, the youngest participant enrolled within the study, supporting the age profiling of this tumour as outlined by Theeler et al (2014). In a SEER (Surveillance, Epidemiology, and End Results) study, of over three thousand adult and paediatric cases, researchers looked at the associated hazard risk of a PA diagnosis across the lifespan (Johnson et al., 2012). A positive correlation between increasing age and associated risk was identified, with the oldest age category of 60+ identified as having the poorest survival. The relative survival associated with the age category (20 – 39 years) that the participant (21 years) from this study corresponded with, identified an observed survival of 93% at 24 months and 89.5% at 60 months. Associated risk with location of the tumour was significantly worse in the adult population for all locations except the cerebellum. This study participant's tumour was localised within the fourth ventricle. Peri-operative complications resulted in the participant having an intra-operative infarct, which complicated recovery and resulted in significant post-operative morbidity.

The differing histological diagnosis obtained by each of the participants has been discussed and highlights the impact location, histology, and demographic variables can have on outcome. The characteristics of the tumour remain only one factor that influences the outcomes of this population of patients.

6.5 Balance

The role of computerised dynamic posturography (CDP) in the assessment of equilibrium and balance has been widely investigated. Two fundamental goals of CDP have been identified (Jacobson et al., 1993) including differentiation between central and peripheral causes of imbalance and to enable appropriate management of patient symptoms by maximising function and limiting the negative impact of the disability. The latter is particularly important in patients with imbalance due to a central lesion, given the potential of a progressive and life threatening clinical course.

Within this study, initial testing of the participants pre-operatively at T1, identified a composite equilibrium score of 58.7 ± 16.2 points. A large degree of variability between participants is highlighted with the large standard deviation, indicating variability in relation to participant's presenting balance and equilibrium. This composite score shows a marked deficit in equilibrium when compared with normal data. In a study comparing SOT equilibrium scores across three ages categories, young (25.2 ± 5.6 years), middle age (50.9 ± 5.7 years) and the elderly (67.4 ± 5.3 years), with this study, a significantly lower composite equilibrium score was attained by the elderly (67.6 ± 6.5 points) when compared with both the young (76.3 ± 5.7 points) and middle-aged (69.9 ± 5.8 points) norms (Liaw et al., 2009). The mean age of the participants in this study was 48.8 ± 15.7 years, indicating most similarity in age with the middle age-group. A notably decreased composite equilibrium is evident in this population (58.7 ± 16.2) when compared with the middle aged norms (69.9 ± 5.8) from the study by Liaw et al (2009). In a study that compared results of CDP and electronystagmography in individuals with peripheral, central or mixed central and peripheral vestibular deficits, a higher prevalence of abnormality was detected in the participants with central involvement (Keim, 1993). These two studies identify both age and central diagnosis as potential contributors to reduced equilibrium scores when compared with normative data.

The SOT was completed at three time-points during the research study; pre-operatively (T1), post-operatively (T2) and at six weeks follow-up (T3). The composite scores obtained for the cohort was 58.7 ± 16.2 at T1, 61.3 ± 11.0 at T2 and 68.1 ± 18.8 at T3. Previous researchers have identified an eight point change in the SOT composite score as a clinically meaningful change (Wrisley et al., 2007). On comparison of the composite scores obtained between T1 and T2 and T2 and T3, an eight point change in equilibrium was not obtained. However, the average composite score obtained between T1 and T3 demonstrated a ten point change in score, highlighting a clinically significant increase in equilibrium, as measured by the SOT at six weeks post-operatively. The hypothesis of the study predicted a reduction in the composite equilibrium scores obtained post-operatively when compared with the pre-operative measurements. However, there was a minor improvement noted in post-operative equilibrium which does not support the proposed hypothesis. This improvement however is not clinically significant when compared with previously established minimal

detectable changes on the SOT (Wrisley et al., 2007). The results of comparison of pre and post-operative SOT scores should be regarded with caution due to differences in the cohorts tested over the two time-points. Only nine participants completed testing post-operatively as compared with pre-operative. The main body of research utilising CDP and the SOT to track changes in balance and equilibrium over time has been in vestibular rehabilitation to evaluate rehabilitation protocols (Meldrum et al., 2015, Pavlou et al., 2004). Within these studies the cohorts are often composed of participants with vestibular deficits resulting from either a peripheral or central lesion. No study is available that has used the SOT to track the impact of a neurosurgical procedure on associated function or outcome. This highlights the novelty of this research. As no pre-existing research is available in this population, it is impossible to draw direct comparison. As previously identified, the normative data that is currently available for SOT composite scores has classified the data according to age categories (Liaw et al., 2009). Due to the limited number of participants in this study, sub-classification of the SOT equilibrium based on age, is impossible.

Within this study ten participants (77%) were diagnosed with a tumour of the cerebellum. Balance deficits associated with cerebellar dysfunction include increased postural sway and an increased potential to fall with the eyes open or shut (Thach and Bastian, 2004). The SOT data collected, relating to the cerebellar participants was distracted from the overall data sample and separate analysis was completed. All ten participants completed the testing pre-operatively. The mean composite equilibrium score obtained was 54.1 ± 15.7 points. Analysis of the whole sample revealed a composite that was four points higher (58.7 ± 16.2), indicating when both the participants with cerebellar and fourth ventricle tumours were collectively analysed, balance function was marginally improved, indicating involvement of the cerebellum had a higher contribution to decreased stability. Only three participants (23%) were diagnosed with fourth ventricle tumours in this study. While involvement of the fourth ventricle has the potential to impair balance due to changes in intra-cranial pressure and associated hydrocephalus (Shoman and Longridge, 2007), no participants within this study population were diagnosed with hydrocephalus on MRI scan at admission. A study investigating the impact of infra-tentorial lesions on falls and postural stability in a cohort of Multiple Sclerosis patients, found that increased falls frequency and reduced static balance was associated with lesions located in the brainstem and middle cerebellar peduncle

(Prosperini et al., 2011), but reduced equilibrium as a result of CNS damage cannot be restricted and localised in its entirety to the exact location of the lesion (Prosperini et al., 2014). While the lesions were located within the cerebellum or the fourth ventricle, the adaptive potential of the tumour due to mechanical and chemical adaptions involved in oncological processes, may have contributed to changes within the tumour surrounding environment, contributing to changes in stability (Blouw et al., 2003). While the pathogenesis of Multiple Sclerosis and brain tumours would differ significantly, both disease processes result in space occupying lesions that could cause compressive, destructive changes to brain tissues.

Condition five and six of the SOT in this study were independently analysed, to determine the participant equilibrium on condition five and six and the associated number of falls that occurred under these testing conditions. As previously outlined condition five tests participants under conditions with eyes closed and unstable platform, while condition six has unstable platform with a sway referenced visual surround. Both the testing conditions aim to distort visual and somatosensory information, with greater deficits on these testing conditions being noted in individuals with deficits of the vestibular system (Di Fabio, 1995). This results in increased reliance on the vestibular system to compensate for the absence or distortion of the visual and somatosensory stimuli on these conditions. The scores obtained reveal reduced equilibrium post-operatively when compared with pre-operative scores and a significant improvement noted by six weeks. A similar trend was noted in the scores obtained for condition six. While a similar pattern in the equilibrium scores across both testing conditions is evident, condition five reveals a greater degree of dysfunction on testing in the pre and post-operative timeframes compared with condition six. Condition five of the SOT is believed to provide the most comprehensive assessment of vestibular function on the SOT (Jacobson et al., 1993). The cerebellum acts as the “adaptive processor” in the monitoring and adjustment of vestibular input through inhibitory modulation, when required, secondary to dysfunction (Khan and Chang, 2013). The localisation of the tumours within the cerebellum of ten participants correlates with the associated vestibular deficits, as highlighted by the dysfunction on condition five and six due to the significant role of the cerebellum in modulating vestibular inputs (Herdman, 2007).

6.6 Gait

Mobility testing within the study utilised the 10m walk test under three different conditions, self-selected walking speed, maximal walking speed and self-selected walking speed with associated horizontal head turns. Walking speed has become a frequently measured outcome in research due to its ease of administration and grading and its ability to predict outcomes such as future health status (Fritz and Lusardi, 2009). Preferred walking speed gives a representation of the individual's preferential speed at which to mobilise and maximum walking speed is the maximum speed at which an individual can ambulate safely (Steffen et al., 2002). Mobility with associated horizontal head turns was also included in the gait testing protocol due to increased difficulties with gait and balance associated with head movement in individuals with vestibular deficits (Marchetti et al., 2008).

Normal gait speed is documented as ranging from 1.2 – 1.4 m/s, which accounts for variations in age, gender, and anthropometrics (Fritz and Lusardi, 2009). On review of the data collected for the study participants, preoperatively (1.3 ± 0.3 m/s) and at six week follow-up (1.3 ± 0.2 m/s), the gait speeds fall within normal ranges. Gait speed immediately post-operatively (0.9 ± 0.4), was outside the range of normal gait speed. This reduction in measured gait speed supports the study hypothesis in which a reduction in gait speed was anticipated, as a direct consequence of the surgery. The findings also highlight the return to pre-surgical walking speed, by the participants, at six weeks post-surgery. The influence of the cerebellum on gait speed and the potential impact of the surgery directly on the cerebellum (Hoogkamer et al., 2015), supports the noted changes in preferred gait speed over time in this cohort.

Maximal gait speeds were collected for the participants, as sensory perturbations have been shown to have a higher impact on gait performance, of healthy subjects, when they walk slowly and less impact when they walk fast (Jahn et al., 2001). A noted deterioration in maximal gait speed was measured post-operatively (1.2 ± 0.4 m/s), with an associated improvement in maximal gait speed at six weeks (1.5 ± 0.3 m/s). In a TBI population, a change of 0.25 m/s was considered a clinically meaningful change in maximal gait speed (Van Loo et al., 2004). When compared with the pre-surgical, maximal gait speed (1.7 ± 0.4), a clinically significant reduced gait speed is evident immediately post-operatively but not at six weeks. Improvements between T2 and T3 were also clinically significant. When

extracting conclusions regarding clinically significant differences in maximal gait speed, the differences in the research populations need to be considered. The noted trend in maximal gait speed changes over the study time-points, supports the study hypothesis.

In a comprehensive study investigating gait speed, based on gender and decade of life, the researchers identified a decrease in gait speed with associated age, and maximal walking speeds showed a more significant decline with age than preferred, self-selected speeds (Bohannon, 1997), in keeping with the results of this study. Direct comparison of both studies is not possible due to variants in the study data collection methods and analysis. In a review of normative self -selected walking speed data, male speeds of 1.18-1.34m/s were identified in a sample of varying age from ten to 79 years (Oberg et al., 1993). While the study contains paediatric cases and a slightly older category of patients, the large age range may account for flexibility in interpretation. The male preferred gait speed in the male cohort of this study fell within the normative rage as identified by Oberg et al (1993). For females the self-selected speed was 1.10 – 1.29 m/s. Within this study the mean female speed falls within this range. A variation in the age categorization of these studies, when compared with this study, prevents direct comparison but observations can be extracted.

6.7 Upper Limb Dexterity

Co-ordination has been defined as “synchronous, spatially coherent movement of two effectors” (Miall et al., 2001), with upper limb dexterity defined as “the fine voluntary movements used to manipulate small objects during a specific task, as measured by the time to complete the task” (Wang et al., 2011). The cerebellum has been shown to be involved in the modulation of upper limb dexterous movements with the characteristics of cerebellar incoordination including hypermetria, dyssynergia, and kinetic tremor (Haggard et al., 1994). The use of the NHPT as a measure of upper limb dexterity in this research study complies with the primary aim of the National Health Institute by using a brief and uniform measure in assessing neurological function.

There were no significant differences in time taken to complete the NHPT across assessment points. Eleven participants (85%) were right handed and discussion will focus on right upper limb dexterity. While there is a minor deterioration in the speed noted immediately post-operatively, a reduced standard deviation highlights greater homogeneity across the testing

scores obtained. Normative data, in relation to speed of execution of the NHPT is available. A study of 340 MS patients, that investigated measurement options for determining the severity of upper limb tremor and ataxia, included a control group of 140 normal participants, to establish normative NHPT data (Erasmus et al., 2001). Dominant hand speed in the control group was 17.81 seconds and non-dominant was 18.49 seconds. A greater than five second difference in execution of the task exists between the participants of this study, at all time-points and the pre-determined adult norms. In a study that looked at establishing normative data for adults, using a commercially available NHPT kit, the authors found a high correlation between age and performance of the NHPT (males: right hand = 0.908, left hand = 0.918; females: right hand = 0.890, left hand = 0.896) (Oxford Grice et al., 2003). Data was not analysed according to hand dominance but collectively analysed as left and right side. Within the study, left hand dominance accounted for less than 10% of the population and the researchers deemed this adequately low to negate the need to analyse the data based on dominance. This study had two participants with left hand dominance, accounting for 14.7% of the study population. A large-scale epidemiological study investigated the NHPT across a wide range of American participants, aged between three and 85 years in an effort to establish age related normative data for the NHPT across the American population (Wang et al., 2015). In a sample of 3,936 participants, the researchers identified a non-linear relationship between dexterity and age and found adults aged 18 to 30 years demonstrating the shortest mean completion time of 19 seconds, while adults aged 70 to 85 demonstrated the slowest completion time, 24.9 seconds. The small number of participants in this study makes sub-analysis based on gender and age difficult due to the restricted volume of data available and as a result direct comparison of the NHPT results in this study must be observed with caution.

The location of the tumours within the posterior fossa in this population of participants was anticipated to impact on the ability to execute upper limb dexterous activities. Eight participants (62%) had their tumour located within the cerebellum, while two of the participants (15%) had the tumour located extra-axially and provided a compressive force on the cerebellar tissues. Researchers have identified functional localizations of the cerebellum and as a result knowledge of the location of the tumour can be linked to anticipated deficits, based on location (Witter and De Zeeuw, 2015). Limb movements are

believed to be controlled by the dentate nucleus, the interpositus nucleus, the intermediate cerebellar cortex and the lateral cerebellar cortex, implying that disruption to tissue in these areas would impact on upper limb motor control (Manto et al., 2012). Lang and Bastian (2002) investigated the involvement of the cerebellum in making a practiced movement more automatic, in a cohort of cerebellar damaged participants and found a reduction in the number of tasks completed, slower hand speed and degradation of the performance with a dual task component when compared to healthy controls. While a notable improvement in the task quality was noted with practice, the cerebellar group showed a more modest gain. The task for completion within their study was the formulation of a figure of eight task with the upper limb, while maintaining upright stance. The task was considered a novel activity ensuring that both the control and cerebellar group would have no prior practice, of such a task. The same would be assumed with the use of the NHPT within our research study, as it would be anticipated that the participants would have had limited exposure to the test prior to involvement in the study. On comparison of mean NHPT scores over the three testing timeframes of the participants with cerebellar tumours (n=10), a reduction in speed of execution was noted immediately post-operatively (T1, 25.6 secs; T2, 23.1 secs, T3, 25.0 secs). Pre-existing data outlining clinically significant changes in NHPT execution time is not available on which to draw comparisons. The study hypothesis anticipated a decrease in the speed of completion of the NHPT post-operatively due to the impact of anticipated surgical trauma. The observed improvement may be explained in part by the immediate decompressive impact of surgery on the cerebellum, relieving associated pressure and reducing symptoms (Gopalakrishnan et al., 2014).

6.8 Dizziness

Dizziness is viewed as a complex neurologic symptom that indicates an imbalance in the perception of balance (Stanton et al., 2007). Within the literature four differing types of dizziness are frequently discussed; vertigo, presyncope, disequilibrium, and nonspecific dizziness (Newman-Toker et al., 2007). Vertigo is linked to vestibular symptoms, presyncope with cardiovascular compromise, disequilibrium with neurological presentations and nonspecific dizziness associated with psychiatric or metabolic disorders. Central causes of dizziness are believed to account for a quarter of all cases of dizziness and tumours are a frequent contributor to central dizziness (Karatas, 2008).

Within this study, dizziness as a pre-operative presenting feature was captured in the participants due to the potential of dizziness occurring as a presenting feature in this population of patients. Seven participants (54%) had dizziness at presentation. This rate of dizziness as a presenting feature is much higher than identified in a profile of 20 cerebellar haemangioblastoma patients in which no patient presented with dizziness (Liao and Huang, 2014). Association of dizziness solely with malignant lesions of the posterior fossa is not supported in the literature. In a case report of an individual with solitary fibrous lesion of the fourth ventricle, dizziness was one of the initial presenting features of this benign lesion (Montano et al., 2010). Of the three participants (23%) who had their lesion located in the fourth ventricle, all three experienced dizziness as a feature at presentation. The potential for ventricular lesions to impact on CSF flow and ultimately intracranial pressure could have contributed to the dizziness experienced by the participants with fourth ventricle lesions (Johnson et al., 2006). This highlights the potential, that dizziness as a pre-operative feature of posterior fossa tumours could be influenced by both the location and histology of the tumour.

The Dizziness Handicap Inventory, a self-report measure of vestibular disease was utilised in this study to monitor the self-perceived disabling features of dizziness, pre and post-operatively (Mutlu and Serbetcioglu, 2013). An eleven point difference is reported between scores pre and immediately post-operatively. This highlights the increase in perceived dizziness, between pre and post-operative testing and supports the hypothesis that the surgical intervention would result in increased levels of dizziness in the participants. While a deterioration in self-perceived dizziness levels is noted, an eleven point change signifies that surgery did not cause an 18 point, significantly meaningful change in self-perceived dizziness as measured by the DHI (Jacobson and Newman, 1990).

DHI scores at T4 (25.1 ± 26.6) show a slight increase when compared with those measured at T3 (24.3 ± 28.9). With an increasing timeframe since surgery, a continued reduction in self-perceived dizziness would be anticipated. The increase in dizziness at T4 may be a result of the evolution of the metastatic lesions diagnosed within the cohort. At T4, DHI data for four of the participants (31% study participants) with metastatic lesions was captured. Metastatic lesions are commonly associated with vasogenic oedema and this in turn plays a pivotal role in enhancing the compressive forces of the tumour (Strugar et al., 1994). The

potential progression of these terminal tumours, with regrowth since the decompressive surgery, may have contributed to the increase in perceived dizziness at six months.

6.9 Post-operative pain

In the current study, pain severity as gathered using the numeric rating scale, the box scale for pain, highlighted the most significant post-operative pain experienced by participants was in the initial post-operative testing period (T2) (3.1 ± 2.6). This initial testing timeframe was determined, as outlined within the methodology as the earliest post-operative period in which the participant felt able to undertake the testing battery and was deemed appropriate by the treating neurosurgeon. Previous research, which has looked at post-operative pain trends in a neurosurgical population, found that reported pain and requests for pain medication, decreased successively over days one, three and five, postoperatively in those receiving burr hole craniotomy surgery (Klimek et al., 2006). This research study also noted a downward trend in post-operative pain levels between T2 (3.1 ± 2.6) and T3 (0.3 ± 0.7). This trend would be anticipated with post-operative natural healing, given that T3 assessments were completed at approximately six weeks post the surgical intervention. Kilmek et al (2006) looked at associated post-operative pain in 13 differing neurosurgical procedures. Craniotomy surgery was revealed to have the second lowest associated post-surgical pain levels of all the interventions investigated. However there are significant differences between the study populations in both studies. Given the tumour locations being investigated in this study, surgical access was restricted to infra-tentorial approaches. Surgical access requiring a sub-occipital or infra-temporal approach has been shown to result in higher post-operative pain levels (Jellish et al., 2006). Noted increased pain levels in individuals undergoing surgical procedures that had sub-occipital or retro-sigmoid access routes suggest that potential trauma to major muscle groups may contribute to the higher pain levels in this population (De Benedittis et al., 1996).

The potential for post-operative pain levels to impact on objective testing was a concern, given the associated risk with this surgical intervention, however only one participant (8%) refused to engage in the T2 testing procedures secondary to post-operative pain. The box scale for pain was not completed as a result but it can be assumed that pain levels would be classified as moderate or severe, given its impact on post-operative engagement in the research protocol. T2 mean participant scores (3.1 ± 2.6) are classified as moderate pain

severity on a numeric rating scale as determined by previous researchers (Gerbershagen et al., 2011). This post-operative complication, coupled with the associated stress of awaiting a histology result, highlights the complexity of recruiting and researching in this population of patients in the acute phase.

A noted minor, non-clinically significant increase in reported pain scores was evident between T3 and T4 (T3; 0.3 ± 0.7; T4; 0.5 ± 1.1). As previously outlined an expected decrease in pain levels would be anticipated in the increasing timeframe from the original surgery. T4 box scale testing was completed by the PI over the phone. While emphasis was placed on pain and how it related to the original post-operative wound, responses may have been provided in relation to a more global concept of pain, which the participant may have been experiencing at that time. Headache pain has been documented as more of a post-surgical issue than surgery site pain in individuals undergoing craniotomy surgery (Klimek et al., 2006) and may have influenced T4 pain results.

Several factors have been associated with influencing levels of perceived post-operative pain including age, sex, expected incision size and surgical procedure (Kalkman et al., 2003). In an orthopaedic study, Thomas et al (1998) identified pre-operative pain levels as a statistically significant predictor of post-operative pain. While the study cohorts differed considerably, it highlights the potential impact pre-surgical headache may have had on post-operative pain outcomes. Nine participants (69%) experienced headache as one of their presenting features. The testing battery did not include a measure to capture this perceived pre-operative pain but may have provided useful information regarding post-operative perception of pain.

6.10 Quality of Life (QOL)

QOL, often termed health related quality of life (HRQOL), measures the impact of disease and the associated treatments on an individual's perceived QOL (Dirven et al., 2014). Individual's own health status and that of their families and friends has been identified as an important factor in people's lives, with the ability to impact on QOL (Bowling, 1995). Limited curative treatment options and associated treatment morbidity, places increased emphasis on the need for appropriate HRQOL brain tumour measures, to assist with evaluation of the risks and benefits in brain tumour management options (van den Bent et

al., 2005). Within the literature, HRQOL has become increasingly recognised as a secondary endpoint in evaluation of brain tumour treatments, in randomized controlled trials (Mauer et al., 2008). Within this study all participants (100%), underwent at least one surgical intervention with seven participants (53.9%) requiring post-surgical radiotherapy and four participants (30.8%) requiring chemotherapy, highlighting the potential risk within this population, of developing negative consequences of treatment, which could impact on HRQOL.

QOL has become an umbrella term, that encompasses several key components that are viewed as integral to the concept of QOL, including physical functioning, health status, perceptions, life conditions, behaviours, happiness, lifestyle and associated symptoms (Moons et al., 2006) The LASA, linear analogue scale assessment, was used as a measure of HRQOL in this study, pre-operatively at T1 and post-operatively at T4. The LASA is a brief measure that is easily administered and has been shown to be a valid measure of HRQOL, in oncology populations (Locke et al., 2007). The LASA captured five of the common features of quality of life, as outlined in the literature (Carr and Higginson, 2001), including overall quality of life, intellectual well-being, spiritual well-being, emotional well-being and physical well-being, pre and post-operatively.

On comparison of the pre and post-surgery QOL data, only one component, physical well-being, showed a one point or greater change in score, pre and post-operatively. Fatigue in brain tumour patients, has been shown to have 40-50% more of a negative impact when compared with general oncology patients (Cormie et al., 2015). Increased levels of fatigue, combined with the trauma of surgery and psychological distress of coping with a brain tumour, may enhance fatigue levels, ultimately having a negative impact on physical ability. In a study investigating the impact of laparoscopic surgery on perceived postoperative fatigue, cardiovascular function, neuro-muscular performance and nutrition rather than psychological factors had the greatest impact on fatigue levels, post-surgery (Christensen et al., 1986). This supports the findings of this study as spiritual, emotional and intellectual well-being, as measured by the LASA showed negligible change, pre and post-operatively, at six months. Failure to complete the LASA immediately post-operatively and at six weeks follow-up may have resulted in the loss of valuable participant related data.

6.11 Loss to follow-up

The nature of the cohort of participants under investigation in this study highlighted a considerable challenge in the ability to monitor and complete follow-up assessments according to the study protocol follow-up timeframes. The rarity of the condition and rigid inclusion and exclusion criteria, restricted the volume of potentially available participants which were recruited to this study. While this rigidity in the protocol resulted in small numbers of included participants (n=13) being identified, it provides a novel insight into a complex neuro-oncology population which has received very limited research attention to date.

Difficulty in the recruitment of participants to healthcare research has become a concern that has resulted in a large degree of effort being employed to assist with identifying the barriers to participation. Several key factors have been identified as determinants in willingness to partake in research including experience of illness in a friend or family member, middle-aged, prior experience of inclusion in medical research, supported use of human subjects in research and belief in ethnic diversity in medical research (Trauth et al., 2000). It has been estimated that in cancer research only 2% of potentially eligible adult patients consent to participate in medical research (Tejeda et al., 1996). Only two individuals (6%) refused to participate in the study which is in direct contradiction with the participation rates as put forward by Tejeda et al (1996). As previously outlined education regarding healthcare and the disease process plays a role in participation in research. While previous exposure to the healthcare system may have assisted with initial recruitment of these participants, the terminal diagnosis created several issues with loss to follow up and subsequently missing data. During the course of this study three participants (24%) had died by the final testing time-point and two participants had significant morbidity which prevented testing (16%).

Loss to follow-up is a major concern in brain tumour research trials (Newberry et al., 2010) and is mirrored in other major populations of research such as TBI (Carroll et al., 2004). Within research, several barriers to the research process have been identified in studies recruiting vulnerable populations such as dying patients. In a study in which the main study population was home hospice patients the main barriers identified were attrition and poor compliance. No difficulties were identified in the initial recruitment of the population

highlighting a willingness of dying patients to participate in research (Dobratz, 2003). While that population of patients were aware of their terminal diagnosis, within this study tumour histology and diagnosis would only have been discovered post-operatively and subsequently post-recruitment and would not have been a factor of influence in original recruitment. In a longitudinal study of palliative cancer and HIV patients, within a sample of 38 cancer patients, only 13% of the recruited sample completed the testing protocol (Sherman et al., 2005). 57% of their data was incomplete due to death and illness which restricted participation. In this study incomplete data is an issue at several time-points throughout the study. At T4 no outcomes are collected for five participants (38%) due to death, morbidity or illness. The discrepancy in retention at follow-up is attributable to the fact this study only had a six month follow-up compared with two years in the Sherman et al (2005) study.

6.12 Mortality

The overall mortality of the study was 23% (3/13) with three participants having died by the final testing timeframe (6 months). Mortality associated with surgical procedures carried out on the posterior fossa is believed to have a higher rate of mortality and significant morbidity when compared with supra-tentorial procedures (Dubey et al., 2009). In a study of 500 patients who underwent posterior fossa surgeries for a variety of diagnosis, CSF leaks, meningitis, wound infection, cranial nerve palsies, cerebellar oedema, hydrocephalus and death were identified as complications that are more frequently observed in infra-tentorial surgical techniques, when compared with supra-tentorial surgery (Dubey et al., 2009). The complication rate within their cohort equated to 31.8% of all surgeries, highlighting the associated risk with posterior fossa surgical approaches.

Two of the participants that died were diagnosed with a metastatic lesion of the brain, with the primary location for both occurring in the lung. Survival with diagnosis of a metastatic brain lesion is considered low, with the median expected survival timeframe generally months rather than years (Gavrilovic and Posner, 2005). Metastatic lesions to the CNS, originating from a lung primary have been speculated to adhere to the “Seed and Soil hypothesis” (Fidler, 2003) as well as dependence on blood flow to assist with transport and subsequently, invasion of the brain tissues (Weiss, 1992). The Seed and Soil hypothesis postulates that the tumour cells (seeds), derived from the primary lesion are transported to and find optimum conditions in the brain tissue, to undergo rapid proliferation (Fidler,

2003). The aggressive nature of metastatic lesions of primary lung origin and the associated poor survival of a metastatic lesion to the brain is highlighted in this study by the death of two participants within the six month follow-up timeframe.

One participant (7%), diagnosed with an atypical choroid plexus papilloma died within the six month follow-up of the study. Although the histological parameters of the tumour are consistent with a WHO grade two histology, the vascular nature of the lesion and the site of origin within the fourth ventricle increases the complexity of access during surgery and the risk of bleeding. In a surgical series of 26 patients with choroid plexus papilloma, two patients undergoing gross total resection died peri-operatively (McGirr et al., 1988). While the participant in this study also underwent a gross total resection, comparison of the surgical outcomes across the two studies is impossible due to limited information documented by McGirr et al (1988) in relation to the peri-surgical complications resulting in death. The participant in this study required two subsequent surgeries due to the development of hydrocephalus secondary to a clot formation post-operatively. The surgical risk associated with the development of hydrocephalus and haemorrhage in this tumour type has been supported in surgical series in the literature (Boyd and Steinbok, 1987), with increased morbidity associated with a posterior fossa location of the tumour (Barbosa et al., 2001).

6.13 Health Care Utilization

The societal burden of treating and managing patients diagnosed with brain tumours, has a significant impact on economies, governments, health systems and individuals (Raizer et al., 2014). In a comprehensive European review of the economic impact of varying brain pathologies, brain tumours were identified as one of the most costly diseases of the brain to treat, with an average spend of approximately €26,000 per patient, in 2010 (Olesen et al., 2012). On analysis of the Irish data within the study, the predicted total cost of brain tumour treatment in Ireland was in excess of €7.5 million, in 2010 (Olesen et al., 2012).

In a review of brain tumour surgical activity within the Republic of Ireland in 2012, 680 intracranial surgeries were completed for primary and secondary brain tumours within Irish neurosurgical centres. Beaumont Hospital executed 552 of the cerebral neuro-oncology surgical interventions, equating to 73% of all the surgeries completed in the country for

adults requiring a surgical intervention due to the presence of a brain tumour (Neuro-oncology annual report, 2012). In 2012, 2,073 neurosurgical procedures were completed in Beaumont Hospital, making brain tumour surgery, 27% of the adult neurosurgical caseload (Beaumont Hospital Annual Report, 2012).

The breakdown of specific surgical and medical modalities, utilised in management of brain tumour patients, has had limited research to date, making cost analysis of the components of brain tumour patient care difficult. In a Swedish study of brain tumour management costs, the number of acute inpatient neurosurgical bed days utilised, based on 1996 data, were 11,687, at a cost of 7.8 million US dollars (Blomqvist et al., 2000). This equates to $667, per bed, per day. The cost of a neurosurgical bed, per day in Beaumont Hospital, during the duration of the study was €286, per bed, per day (Beaumont Hospital Finance Report, 2015). Costings, for an intensive therapy unit (ITU) bed, per day were €1873 (General Intensive Care and Richmond Intensive Care Audit, 2014). 257 neurosurgical bed days were utilised by the study cohort, 221 days in ward based beds and 36 in ITU. This equates to a total cost of €130,634, to maintain the study participants in acute neurosurgical beds, in Beaumont Hospital, over the study duration.

The average length of stay, across all departments of Beaumont Hospital, in 2012 was 9.9 days (Beaumont Hospital Annual Report, 2012) and 9.25 days in 2013 (Beaumont Hospital annual report, 2013). Within this study, the average length of stay of the participants, in an acute neurosurgical bed, was 19.8 ± 21.6 days. This figure is higher than the LOS, for a population of brain tumour patients undergoing a craniotomy for brain tumour, in an academic teaching hospital in Maryland, USA (Long et al., 2003). The average LOS was 9.9 days, considerably shorter than that seen in the study participants. The discrepancy may be due to the differences between the health service delivery systems in Ireland and the USA and the localisation of all tumours in this study within the posterior fossa. While a modest trend in decreased average length of stay (LOS) is notable between the years 2012 and 2013 for the hospital, participants of this study had considerably longer LOS. While total average LOS for the hospital over the duration of the study is not available, the longer length of stay in this cohort, when compared with previous hospital averages, reflects the complexity of the diagnosis. Potential morbidity associated with diagnosis of a brain tumour (Mukand et al., 2001) and increased speciality MDT involvement, may contribute to this increased

demand on inpatient resources from this population of patients (Guilfoyle et al., 2011). Best practice in the management of brain tumour patients supports a multidisciplinary team approach to manage the diverse and complex needs of the brain tumour patient, which ultimately leads to longer hospital stays to allow the patient access to required services and reduce the burden of further travel to the hospital, post discharge (Eichler and Loeffler, 2007).

The protocol and testing battery completed as part of this study was conducted in full by the PI, a senior neurosurgical physiotherapist. The estimated timeframe for completion of each testing procedure was one hour. The protocol outlined four timeframes for the testing of each participant, with an associated four hours of senior therapist time, equating to 52 hours of dedicated time to the participants as part of the protocol. Based on the cost of a senior physiotherapy salary per hour, implementation of this research protocol cost approximately €1,800, in physiotherapy time resources. Given the complexity of the presenting features and risk of surgical morbidity, careful and comprehensive examination of this population is essential to provide optimum care. The implementation of a testing battery for this population, based on the study protocol could potentially reduce service cost. Early identification of surgery associated deficits would allow for optimally timed, rehabilitation interventions, with the potential to reduce the number of inpatient bed days required, reducing overall cost to the hospital and ultimately, the Health Service Executive (HSE).

6.14 Limitations

Several limitations were encountered during the course of this research study and have been mentioned and discussed throughout this chapter. This section will give a summary of the main limitations experienced.

The population of brain tumour patients being investigated were considered a rare cohort, with the potential numbers available to recruit to the study expected to be small. This proved to be the case, with only thirteen participants being recruited for participation. The small sample size limits the ability to extract robust conclusions in relation to the results of the study. While the numbers are small, a valuable catalogue of data relating to this

complex cohort is now available, profiling the impact of surgery on a variety of tumour associated impairments.

Access to potential participants was often identified as a barrier to recruitment. A large volume of potential participants that presented to Beaumont Hospital were transferred under emergency procedures and received surgery prior to consideration for inclusion. The imminent surgery of these patients highlights the potentially critical nature of those with a posterior fossa tumour. This study protocol aimed to gather data on more functionally able participants, which formed a small subset of this population, based on excluded data. Care must be heeded on the extrapolation of patterns in relation to this population of patients, as more critical cases may never have had the potential for inclusion.

Measurement variability was an issue throughout the research project. Variations in relation to patient access, post-operative complications and morbidity prevented standardisation of the testing protocol. Several participants failed to complete the full testing procedure due to morbidity and mortality. While every effort was made to standardise the testing procedure, the acute and critical nature of this population limited protocol execution. These methodological limitations however, provided valuable data in relation to the complexities in management and researching this population.

The data gathered excluded tumours originating in the internal auditory meatus. This is a common site of origin for vestibular schwannomas. This tumour type has a tendency to grow and migrate out into the cerebello-pontine angle and can cause compressive force on the cerebellum and brainstem. Technically classified as a posterior fossa lesion, presentation and surgical management of this tumour type differs significantly to those discussed in this study. Exclusion of participants with this tumour type from potential inclusion, limits the conclusions that be extracted, in relation to all posterior fossa tumours that occurred in an eighteen month period, in Beaumont Hospital.

Within this research study the objective testing battery, incorporating the Equitest, 10m walking tests and NHPT was not completed at the six month follow-up. This component of the protocol was designed to reduce the burden on the participants as travel back to Beaumont Hospital would not be required. As attendance in Beaumont was not guaranteed at this stage of the participants neurosurgical management and the potential of medical

deterioration at six months a phone follow-up to administer the subjective outcome measures was deemed appropriate to monitor patient status. While completion of the full testing battery at six months would have provided useful data, increased participant burden resulted in its exclusion from the finalised protocol.

The quality of life data, using the LASA scale, was only completed by the participants pre-operatively and at six months follow-up. Exclusion of the scale as a component of the testing battery at Tp two and three was to reduce participant burden but may have provided useful information in relation to peri-operative QOL in this population.

The data captured in relation to the physiotherapy involvement in this population of patients did not capture the rehabilitation techniques utilised to treat the study participants, post-operatively. Analysis of the treatments provided would have enhanced the catalogue of data available in relation to this cohort. The lack of data collection in relation to the rehabilitation provided to the study participants was based on logistical limitations including time restrictions and study execution on a part-time basis. Retrospective analysis of the rehabilitation techniques used could be undertaken as a second stage research project in the future, to further enhance the catalogue of data in relation to this population.

Loss to follow-up of participants was a major limitation of this study and resulted in reduced levels of data available for analysis. Given the small initial cohort numbers, this loss of follow-up data diluted the results obtained and the ability to extrapolate more robust conclusions. While loss of data is a limitation of the study, the morbidity and mortality resulting in incomplete datasets cannot be ignored as a very relevant feature of this population of neuro-oncology patients.

The small volume of participants recruited to the study also limited the type of statistical analysis that could be utilised in the study. The statistical analysis in the study has been based solely on descriptive statistics. To adequately analyse the impact of surgery on balance, gait, upper limb dexterity and dizziness in this population, a larger population of patients, recruited over a longer period of time would be required, to allow for the use of inferential statistics.

6.15 Considerations for Future Research

During the period of recruitment for the research study, thirty-one participants were excluded from the study for a variety of reasons. Difficulty in the recruitment of participants to healthcare research has become a concern that has resulted in a large degree of research being conducted to assist with identifying the barriers to participation. Several key factors have been identified as determinants in willingness to partake in research, including experience of illness in a friend or family member, being middle-aged, prior experience of inclusion in medical research, supported use of human subjects in research and belief in ethnic diversity in medical research (Trauth et al., 2000). Misconceptions, fear, and a lack of appropriate information are also believed to limit participation in clinical research (Lawrence, 1990). It has been estimated that in cancer research, only 2% of potentially eligible adult patients consent to participate in medical research (Tejeda et al., 1996). Careful consideration of the pre-existing barriers to research and in particular cancer research, would assist with the establishment of research protocols that would accommodate maximum recruitment, in future brain tumour studies.

The limited research available in this cohort and the difficulties identified in recruitment, make optimal protocol design for research in this population difficult. The limited catalogue of available research in this population highlights the need for further investigation in this cohort. This research study provides preliminary data on a rare population but several potential difficulties in the implementation of a second stage study exist. In chapter four, the significant lack of quality evidence evaluating rehabilitation in this population was identified. The conclusions drawn in the systematic review highlighted the need for further research to be completed to enhance the pre-existing catalogue. Small observational studies evaluating a particular rehabilitation approach might be more appropriate, in the initial phase. The use of smaller observation studies would enhance the available research catalogue available in relation to this population on which to structure more robust protocols. Components of the testing battery used in this prospective study could be used as the framework for a methodology, evaluating particular rehabilitation approaches. Prospective evaluation of treatment approaches for use in this population would consolidate the catalogue of evidence available in relation to surgery and rehabilitation in this population of patients.

Chapter 7: Conclusion

The primary aim of this study was to investigate the impact of a surgical intervention on balance, gait, upper limb dexterity and dizziness in patients with posterior fossa tumours. The study hypothesis proposed a noted decrease in balance, walking speed, upper limb dexterity and an increase in dizziness, post-operatively, when compared with their pre-operative status. The results obtained for the primary outcome, equilibrium and balance, did not support the hypothesis, with a noted improvement in balance and equilibrium post-operatively. While a modest improvement was observed immediately post-operatively, it was not considered a clinically significant improvement. A clinically significant improvement was noted in balance and equilibrium by six weeks follow-up, when compared with pre-operative status. Results of the secondary outcomes, gait speed, upper limb dexterity and self-reported dizziness, supported the study hypothesis, showing a decline in function post-operatively. For each of the 10m walk testing conditions, a deterioration in function was noted post-operatively, with a significant improvement in gait speed captured by the six week follow-up. A similar pattern was noted for the NHPT when executed for the right upper limb but by six week follow-up, left upper limb dexterity had not improved when compared with the post-operative results. Participants self-perceived dizziness levels improved by six week review, with a very minor deterioration noted by six month follow-up. At both six weeks and six months post-operatively, self-perceived dizziness had not returned to pre-operative status. The results of the testing battery utilised in this study highlight the impairments associated with a tumour of this region of the brain and the comprehensive assessment that should be conducted as part of routine care on which to formulate adequate and comprehensive treatment programmes.

The secondary aims of the study were to profile participant and tumour characteristics of the study participants. The profile presented of the included participants, provided confirmation of the rarity of the condition under investigation, the risk of malignancy associated with a tumour of this portion of the brain and the associated mortality and morbidity. The study has provided a profile of the characteristics associated with a tumour of this portion of the brain and will assist physiotherapists with pattern recognition and symptomology, on which to formulate clinical decisions.

In an era of health care volatility, with a demand for cost-effectiveness and consumer satisfaction, physiotherapists along with all members of the multi-disciplinary team, need to support clinical decisions with evidence based research. This research study has provided novel, comprehensive research into a neuro-oncological population that has received limited research to date. As previously outlined, with increasing numbers of patients presenting with tumours in this location of the brain, this research will provide a framework for physiotherapists, on which to formulate assessments and rehabilitation programmes to maximise recovery and function.

Implementation of future research studies in this population needs to consider the morbidity and mortality associated with diagnosis of a posterior fossa tumour, as identified in this study. The results of this study highlighted the impact of surgery on outcome and provides novel information regarding the devastating physical consequences of the diagnosis and associated surgery. Future research direction involving this population should consider the exploration of qualitative research methods to explore patient perceptions of rehabilitation and physiotherapy confidence in the management of this complex population. Further insight into the patient's perspective could assist with the tailoring of meaningful future quantitative protocols and will potentially assist with participant recruitment and reduce attrition.

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Appendix 1: Pubmed search-string for systematic review

PUBMED

(((((((("posterior fossa tumour"[All Fields] OR "infratentorial neoplasms"[MeSH Terms] OR ("infratentorial"[All Fields] AND "neoplasms"[All Fields]) OR "infratentorial neoplasms"[All Fields] OR ("posterior"[All Fields] AND "fossa"[All Fields] AND "tumor"[All Fields]) OR "posterior fossa tumor"[All Fields]) AND "infratentorial neoplasms"[MeSH Terms]) OR (("cerebellar neoplasms"[MeSH Terms] OR ("cerebellar"[All Fields] AND "neoplasms"[All Fields]) OR "cerebellar neoplasms"[All Fields] OR ("cerebellar"[All Fields] AND "neoplasm"[All Fields]) OR "cerebellar neoplasm"[All Fields]) AND "cerebellar neoplasms"[MeSH Terms])) OR (("brain stem neoplasms"[MeSH Terms] OR ("brain"[All Fields] AND "stem"[All Fields] AND "neoplasms"[All Fields]) OR "brain stem neoplasms"[All Fields] OR ("brainstem"[All Fields] AND "neoplasm"[All Fields]) OR "brainstem neoplasm"[All Fields]) AND "brain stem neoplasms"[MeSH Terms])) AND (("rehabilitation"[Subheading] OR "rehabilitation"[All Fields] OR "rehabilitation"[MeSH Terms]) AND "rehabilitation"[MeSH Terms])) OR (((((("posterior fossa tumour"[All Fields] OR "infratentorial neoplasms"[MeSH Terms] OR ("infratentorial"[All Fields] AND "neoplasms"[All Fields]) OR "infratentorial neoplasms"[All Fields] OR ("posterior"[All Fields] AND "fossa"[All Fields] AND "tumor"[All Fields]) OR "posterior fossa tumor"[All Fields]) AND "infratentorial neoplasms"[MeSH Terms]) OR (("cerebellar neoplasms"[MeSH Terms] OR ("cerebellar"[All Fields] AND "neoplasms"[All Fields]) OR "cerebellar neoplasms"[All Fields] OR ("cerebellar"[All Fields] AND "neoplasm"[All Fields]) OR "cerebellar neoplasm"[All Fields]) AND "cerebellar neoplasms"[MeSH Terms])) OR (("brain stem neoplasms"[MeSH Terms] OR ("brain"[All Fields] AND "stem"[All Fields] AND "neoplasms"[All Fields]) OR "brain stem neoplasms"[All Fields] OR ("brainstem"[All Fields] AND "neoplasm"[All Fields]) OR "brainstem neoplasm"[All Fields]) AND "brain stem neoplasms"[MeSH Terms])) AND (("postural balance"[MeSH Terms] OR ("postural"[All Fields] AND "balance"[All Fields]) OR "postural balance"[All Fields] OR ("balance"[All Fields] AND "postural"[All Fields])) AND "postural balance"[MeSH Terms]))) OR (((((("posterior fossa tumour"[All Fields] OR "infratentorial neoplasms"[MeSH Terms] OR ("infratentorial"[All Fields] AND "neoplasms"[All Fields]) OR "infratentorial neoplasms"[All Fields] OR ("posterior"[All Fields] AND "fossa"[All Fields] AND "tumor"[All Fields]) OR "posterior fossa tumor"[All Fields]) AND "infratentorial neoplasms"[MeSH Terms]) OR (("cerebellar neoplasms"[MeSH Terms] OR ("cerebellar"[All Fields] AND "neoplasms"[All Fields]) OR "cerebellar neoplasms"[All Fields] OR ("cerebellar"[All Fields] AND "neoplasm"[All Fields]) OR "cerebellar neoplasm"[All Fields]) AND "cerebellar neoplasms"[MeSH Terms])) OR (("brain stem neoplasms"[MeSH Terms] OR ("brain"[All Fields] AND "stem"[All Fields] AND "neoplasms"[All Fields]) OR "brain stem neoplasms"[All Fields] OR ("brainstem"[All Fields] AND "neoplasm"[All Fields]) OR "brainstem neoplasm"[All Fields]) AND "brain stem neoplasms"[MeSH Terms])) AND (("gait disorders, neurologic"[MeSH Terms] OR ("gait"[All Fields] AND "disorders"[All Fields] AND "neurologic"[All Fields]) OR "neurologic gait disorders"[All Fields] OR ("gait"[All Fields] AND "disorders"[All Fields] AND "neurologic"[All Fields]) OR "gait disorders, neurologic"[All Fields]) AND "gait disorders, neurologic"[MeSH Terms]))) OR (((((("posterior fossa tumour"[All

Fields] OR "infratentorial neoplasms"[MeSH Terms] OR ("infratentorial"[All Fields] AND "neoplasms"[All Fields]) OR "infratentorial neoplasms"[All Fields] OR ("posterior"[All Fields] AND "fossa"[All Fields] AND "tumor"[All Fields]) OR "posterior fossa tumor"[All Fields]) AND "infratentorial neoplasms"[MeSH Terms]) OR (("cerebellar neoplasms"[MeSH Terms] OR ("cerebellar"[All Fields] AND "neoplasms"[All Fields]) OR "cerebellar neoplasms"[All Fields] OR ("cerebellar"[All Fields] AND "neoplasm"[All Fields]) OR "cerebellar neoplasm"[All Fields]) AND "cerebellar neoplasms"[MeSH Terms])) OR (("brain stem neoplasms"[MeSH Terms] OR ("brain"[All Fields] AND "stem"[All Fields] AND "neoplasms"[All Fields]) OR "brain stem neoplasms"[All Fields] OR ("brainstem"[All Fields] AND "neoplasm"[All Fields]) OR "brainstem neoplasm"[All Fields]) AND "brain stem neoplasms"[MeSH Terms])) AND (("vertigo"[MeSH Terms] OR "vertigo"[All Fields]) AND "vertigo"[MeSH Terms]))) OR (((((("posterior fossa tumour"[All Fields] OR "infratentorial neoplasms"[MeSH Terms] OR ("infratentorial"[All Fields] AND "neoplasms"[All Fields]) OR "infratentorial neoplasms"[All Fields] OR ("posterior"[All Fields] AND "fossa"[All Fields] AND "tumor"[All Fields]) OR "posterior fossa tumor"[All Fields]) AND "infratentorial neoplasms"[MeSH Terms]) OR (("cerebellar neoplasms"[MeSH Terms] OR ("cerebellar"[All Fields] AND "neoplasms"[All Fields]) OR "cerebellar neoplasms"[All Fields] OR ("cerebellar"[All Fields] AND "neoplasm"[All Fields]) OR "cerebellar neoplasm"[All Fields]) AND "cerebellar neoplasms"[MeSH Terms])) OR (("brain stem neoplasms"[MeSH Terms] OR ("brain"[All Fields] AND "stem"[All Fields] AND "neoplasms"[All Fields]) OR "brain stem neoplasms"[All Fields] OR ("brainstem"[All Fields] AND "neoplasm"[All Fields]) OR "brainstem neoplasm"[All Fields]) AND "brain stem neoplasms"[MeSH Terms])) AND (("vertigo"[MeSH Terms] OR "vertigo"[All Fields] OR "dizziness"[All Fields] OR "dizziness"[MeSH Terms]) AND ("vertigo"[MeSH Terms] OR "dizziness"[MeSH Terms])))) OR (((((("posterior fossa tumour"[All Fields] OR "infratentorial neoplasms"[MeSH Terms] OR ("infratentorial"[All Fields] AND "neoplasms"[All Fields]) OR "infratentorial neoplasms"[All Fields] OR ("posterior"[All Fields] AND "fossa"[All Fields] AND "tumor"[All Fields]) OR "posterior fossa tumor"[All Fields]) AND "infratentorial neoplasms"[MeSH Terms]) OR (("cerebellar neoplasms"[MeSH Terms] OR ("cerebellar"[All Fields] AND "neoplasms"[All Fields]) OR "cerebellar neoplasms"[All Fields] OR ("cerebellar"[All Fields] AND "neoplasm"[All Fields]) OR "cerebellar neoplasm"[All Fields]) AND "cerebellar neoplasms"[MeSH Terms])) OR (("brain stem neoplasms"[MeSH Terms] OR ("brain"[All Fields] AND "stem"[All Fields] AND "neoplasms"[All Fields]) OR "brain stem neoplasms"[All Fields] OR ("brainstem"[All Fields] AND "neoplasm"[All Fields]) OR "brainstem neoplasm"[All Fields]) AND "brain stem neoplasms"[MeSH Terms])) AND (("quality of life"[MeSH Terms] OR ("quality"[All Fields] AND "life"[All Fields]) OR "quality of life"[All Fields]) AND "quality of life"[MeSH Terms]))

Appendix 2: Sciverse/Scopus search-string

SCIVERSE/SCOPUS

((((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**physiotherapy**))) OR (((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**physical therapy**))) OR (((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**balance**))) OR (((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**rehabilitation**))) OR (((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**"gait disorders"**))) OR (((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**vertigo**))) OR (((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**dizziness**)))) OR (((ALL(**"posterior fossa tumour"**)) OR (ALL(**brainstem neoplasm**)) OR (ALL(**cerebellar neoplasm**))) AND (ALL(**"quality of life"**)))

Appendix 3: Care Checklist outlining study quality of Ada et al (2009), included in the systematic review

CARE Checklist (2013) of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Page
Title	**1**	The words "case report" should be in the title along with the area of focus	Y
Key Words	**2**	2 to 5 key words that identify areas covered in this case report	Y
Abstract	**3a**	Introduction—What is unique about this case? What does it add to the medical literature?	Y
	3b	The main symptoms of the patient and the important clinical findings	Y
	3c	The main diagnoses, therapeutics interventions, and outcomes	Y
	3d	Conclusion—What are the main "take-away" lessons from this case?	Y
Introduction	**4**	One or two paragraphs summarizing why this case is unique with references	Y
Patient Information	**5a**	De-identified demographic information and other patient specific information	Y
	5b	Main concerns and symptoms of the patient	Y
	5c	Medical, family, and psychosocial history including relevant genetic information (also see timeline)	Y
	5d	Relevant past interventions and their outcomes	Y
Clinical Findings	**6**	Describe the relevant physical examination (PE) and other significant clinical findings	Y
Timeline	**7**	Important information from the patient's history organized as a timeline	Y
Diagnostic Assessment	**8a**	Diagnostic methods (such as PE, laboratory testing, imaging, surveys)	Y
	8b	Diagnostic challenges (such as access, financial, or cultural)	Y
	8c	Diagnostic reasoning including other diagnoses considered	N
	8d	Prognostic characteristics (such as staging in oncology) where applicable	Y
Therapeutic Intervention	**9a**	Types of intervention (such as pharmacologic, surgical, preventive, self-care)	Y
	9b	Administration of intervention (such as dosage, strength, duration)	Y
	9c	Changes in intervention (with rationale)	N
Follow-up and Outcomes	**10a**	Clinician and patient-assessed outcomes (when appropriate)	Y
	10b	Important follow-up diagnostic and other test results	Y
	10c	Intervention adherence and tolerability (How was this assessed?)	Y
	10d	Adverse and unanticipated events	N
Discussion	**11a**	Discussion of the strengths and limitations in your approach to this case	Y
	11b	Discussion of the relevant medical literature	Y
	11c	The rationale for conclusions (including assessment of possible causes)	Y
	11d	The primary "take-away" lessons of this case report	Y
Patient Perspective	**12**	When appropriate the patient should share their perspective on the treatments they received	N
Informed Consent	**13**	Did the patient give informed consent? Please provide if requested	Yes ☑ No ☐

Appendix 4: Care Checklist outlining study quality of Betker et al (2006), included in the systematic review

CARE Checklist (2013) of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Page
Title	1	The words "case report" should be in the title along with the area of focus	Y
Key Words	2	2 to 5 key words that identify areas covered in this case report	Y
Abstract	3a	Introduction—What is unique about this case? What does it add to the medical literature?	Y
	3b	The main symptoms of the patient and the important clinical findings	Y
	3c	The main diagnoses, therapeutics interventions, and outcomes	Y
	3d	Conclusion—What are the main "take-away" lessons from this case?	Y
Introduction	4	One or two paragraphs summarizing why this case is unique with references	Y
Patient Information	5a	De-identified demographic information and other patient specific information	Y
	5b	Main concerns and symptoms of the patient	Y
	5c	Medical, family, and psychosocial history including relevant genetic information (also see timeline)	N
	5d	Relevant past interventions and their outcomes	Y
Clinical Findings	6	Describe the relevant physical examination (PE) and other significant clinical findings	Y
Timeline	7	Important information from the patient's history organized as a timeline	Y
Diagnostic Assessment	8a	Diagnostic methods (such as PE, laboratory testing, imaging, surveys)	Y
	8b	Diagnostic challenges (such as access, financial, or cultural)	N
	8c	Diagnostic reasoning including other diagnoses considered	N
	8d	Prognostic characteristics (such as staging in oncology) where applicable	N
Therapeutic Intervention	9a	Types of intervention (such as pharmacologic, surgical, preventive, self-care)	Y
	9b	Administration of intervention (such as dosage, strength, duration)	Y
	9c	Changes in intervention (with rationale)	Y
Follow-up and Outcomes	10a	Clinician and patient-assessed outcomes (when appropriate)	Y
	10b	Important follow-up diagnostic and other test results	N
	10c	Intervention adherence and tolerability (How was this assessed?)	Y
	10d	Adverse and unanticipated events	N
Discussion	11a	Discussion of the strengths and limitations in your approach to this case	Y
	11b	Discussion of the relevant medical literature	Y
	11c	The rationale for conclusions (including assessment of possible causes)	Y
	11d	The primary "take-away" lessons of this case report	Y
Patient Perspective	12	When appropriate the patient should share their perspective on the treatments they received	N
Informed Consent	13	Did the patient give informed consent? Please provide if requested	Yes ☐ No ☑

Appendix 5: Care Checklist outlining study quality of Cremer (1998), included in the systematic review

CARE Checklist (2013) of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Page
Title	1	The words "case report" should be in the title along with the area of focus	Y
Key Words	2	2 to 5 key words that identify areas covered in this case report	N
Abstract	3a	Introduction—What is unique about this case? What does it add to the medical literature?	N
	3b	The main symptoms of the patient and the important clinical findings	N
	3c	The main diagnoses, therapeutics interventions, and outcomes	N
	3d	Conclusion—What are the main "take-away" lessons from this case?	N
Introduction	4	One or two paragraphs summarizing why this case is unique with references	N
Patient Information	5a	De-identified demographic information and other patient specific information	Y
	5b	Main concerns and symptoms of the patient	Y
	5c	Medical, family, and psychosocial history including relevant genetic information (also see timeline)	Y
	5d	Relevant past interventions and their outcomes	N
Clinical Findings	6	Describe the relevant physical examination (PE) and other significant clinical findings	N
Timeline	7	Important information from the patient's history organized as a timeline	N
Diagnostic Assessment	8a	Diagnostic methods (such as PE, laboratory testing, imaging, surveys)	N
	8b	Diagnostic challenges (such as access, financial, or cultural)	N
	8c	Diagnostic reasoning including other diagnoses considered	N
	8d	Prognostic characteristics (such as staging in oncology) where applicable	N
Therapeutic Intervention	9a	Types of intervention (such as pharmacologic, surgical, preventive, self-care)	N
	9b	Administration of intervention (such as dosage, strength, duration)	N
	9c	Changes in intervention (with rationale)	N
Follow-up and Outcomes	10a	Clinician and patient-assessed outcomes (when appropriate)	N
	10b	Important follow-up diagnostic and other test results	N
	10c	Intervention adherence and tolerability (How was this assessed?)	N
	10d	Adverse and unanticipated events	N
Discussion	11a	Discussion of the strengths and limitations in your approach to this case	N
	11b	Discussion of the relevant medical literature	N
	11c	The rationale for conclusions (including assessment of possible causes)	Y
	11d	The primary "take-away" lessons of this case report	Y
Patient Perspective	12	When appropriate the patient should share their perspective on the treatments they received	Y
Informed Consent	13	Did the patient give informed consent? Please provide if requested	Yes ☐ No ☒

Appendix 6: Care Checklist outlining study quality of Gill-Body (1997), included in the systematic review

CARE Checklist (2013) of information to include when writing a case report

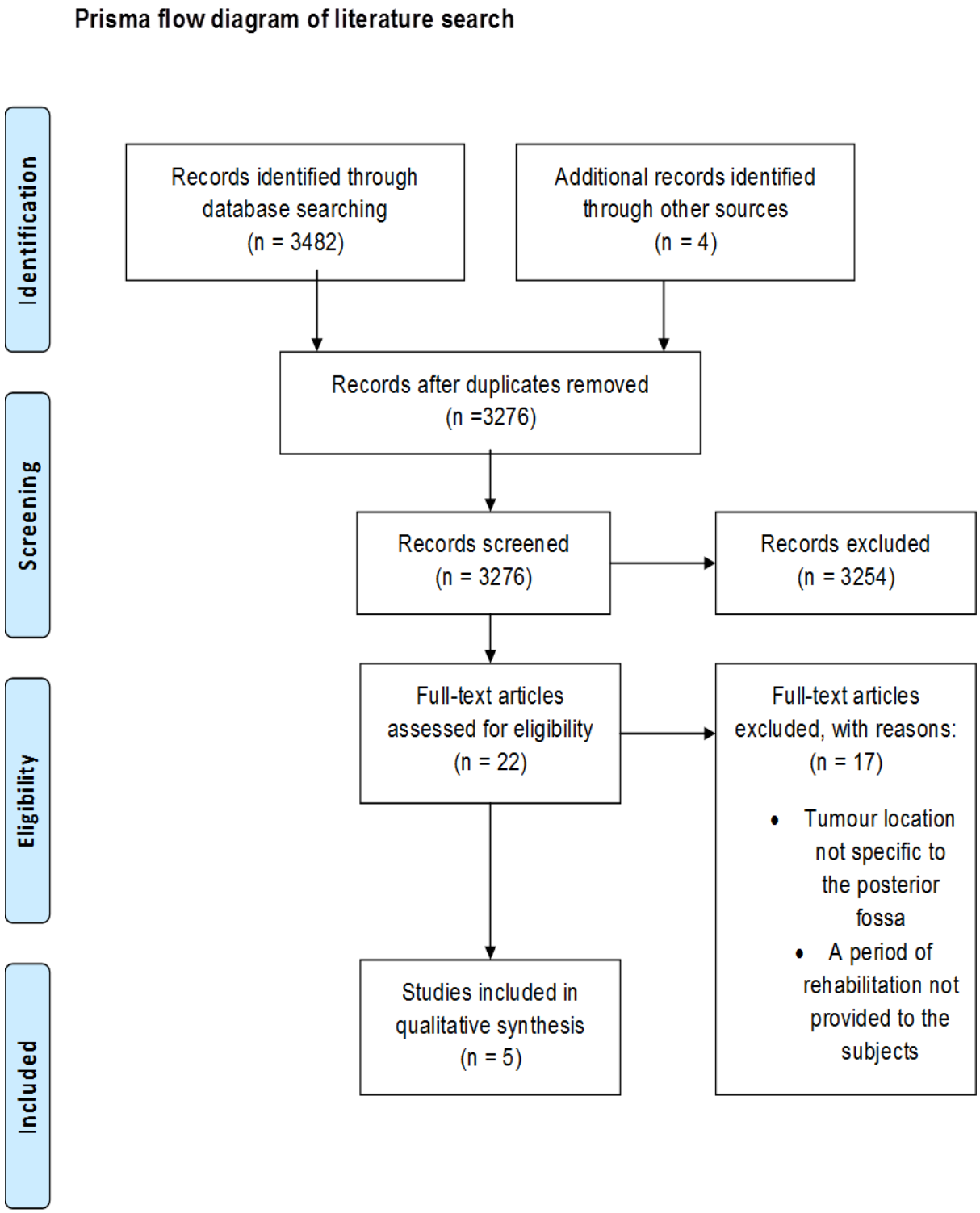
Topic	Item	Checklist item description	Reported on Page
Title	1	The words "case report" should be in the title along with the area of focus	Y
Key Words	2	2 to 5 key words that identify areas covered in this case report	Y
Abstract	3a	Introduction—What is unique about this case? What does it add to the medical literature?	N
	3b	The main symptoms of the patient and the important clinical findings	Y
	3c	The main diagnoses, therapeutics interventions, and outcomes	Y
	3d	Conclusion—What are the main "take-away" lessons from this case?	Y
Introduction	4	One or two paragraphs summarizing why this case is unique with references	Y
Patient Information	5a	De-identified demographic information and other patient specific information	Y
	5b	Main concerns and symptoms of the patient	Y
	5c	Medical, family, and psychosocial history including relevant genetic information (also see timeline)	Y
	5d	Relevant past interventions and their outcomes	Y
Clinical Findings	6	Describe the relevant physical examination (PE) and other significant clinical findings.	Y
Timeline	7	Important information from the patient's history organized as a timeline	Y
Diagnostic Assessment	8a	Diagnostic methods (such as PE, laboratory testing, imaging, surveys).	Y
	8b	Diagnostic challenges (such as access, financial, or cultural)	Y
	8c	Diagnostic reasoning including other diagnoses considered	N/A
	8d	Prognostic characteristics (such as staging in oncology) where applicable	Y
Therapeutic Intervention	9a	Types of intervention (such as pharmacologic, surgical, preventive, self-care)	Y
	9b	Administration of intervention (such as dosage, strength, duration)	Y
	9c	Changes in intervention (with rationale)	Y
Follow-up and Outcomes	10a	Clinician and patient-assessed outcomes (when appropriate)	Y
	10b	Important follow-up diagnostic and other test results	Y
	10c	Intervention adherence and tolerability (How was this assessed?)	Y
	10d	Adverse and unanticipated events	N
Discussion	11a	Discussion of the strengths and limitations in your approach to this case	Y
	11b	Discussion of the relevant medical literature	Y
	11c	The rationale for conclusions (including assessment of possible causes)	Y
	11d	The primary "take-away" lessons of this case report	Y
Patient Perspective	12	When appropriate the patient should share their perspective on the treatments they received	N/A
Informed Consent	13	Did the patient give informed consent? Please provide if requested	Yes ☐ No ☑

Appendix 7: Care Checklist outlining study quality of Karakaya et al (2000), included in the systematic review

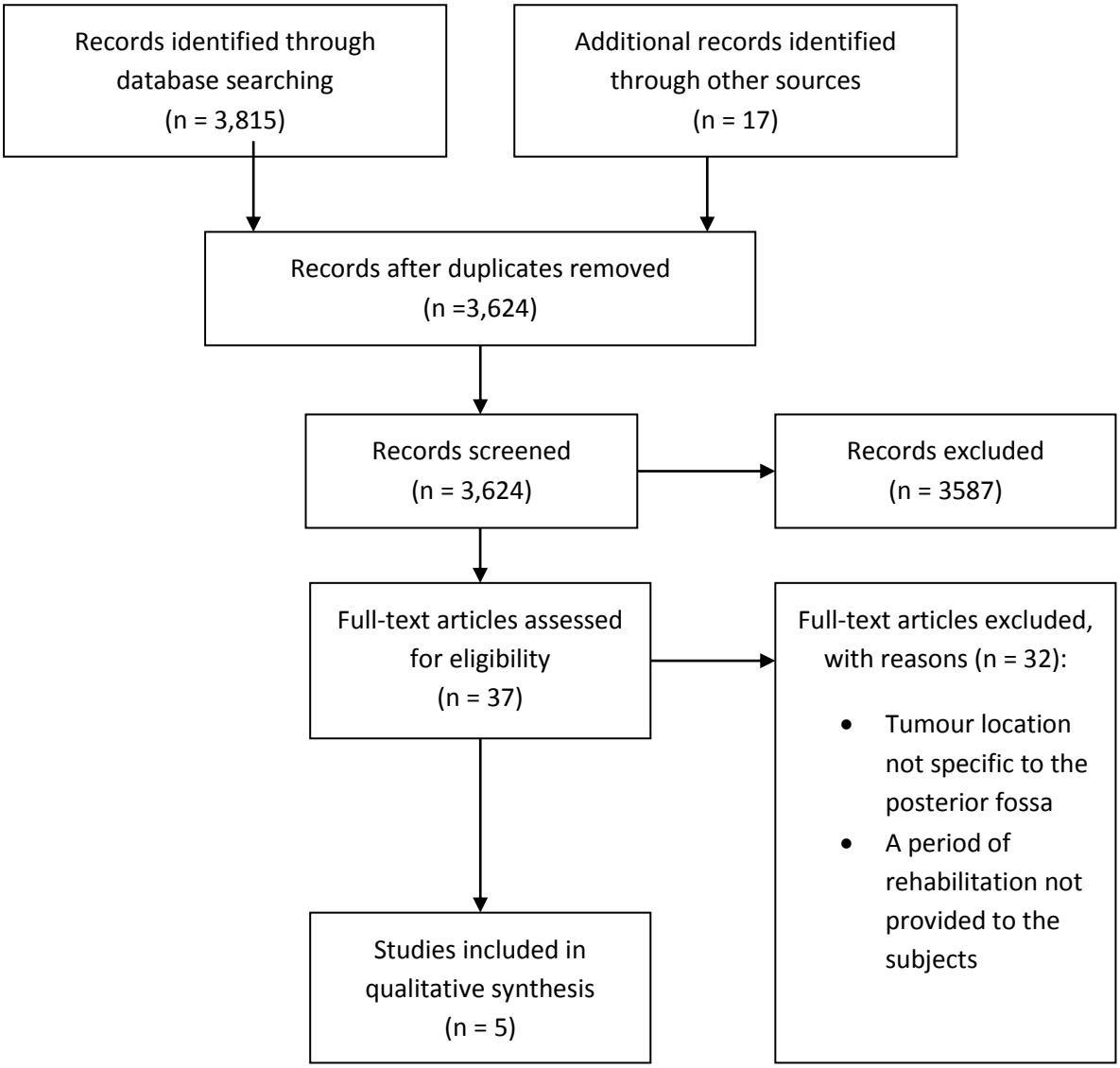
CARE Checklist (2013) of information to include when writing a case report

Topic	Item	Checklist item description	Reported on Page
Title	1	The words "case report" should be in the title along with the area of focus	N
Key Words	2	2 to 5 key words that identify areas covered in this case report	Y
Abstract	3a	Introduction—What is unique about this case? What does it add to the medical literature?	Y
	3b	The main symptoms of the patient and the important clinical findings	N
	3c	The main diagnoses, therapeutics interventions, and outcomes	Y
	3d	Conclusion—What are the main "take-away" lessons from this case?	Y
Introduction	4	One or two paragraphs summarizing why this case is unique with references	Y
Patient Information	5a	De-identified demographic information and other patient specific information	N
	5b	Main concerns and symptoms of the patient	N
	5c	Medical, family, and psychosocial history including relevant genetic information (also see timeline)	N
	5d	Relevant past interventions and their outcomes	Y
Clinical Findings	6	Describe the relevant physical examination (PE) and other significant clinical findings.	Y
Timeline	7	Important information from the patient's history organized as a timeline	N
Diagnostic Assessment	8a	Diagnostic methods (such as PE, laboratory testing, imaging, surveys).	Y
	8b	Diagnostic challenges (such as access, financial, or cultural)	N
	8c	Diagnostic reasoning including other diagnoses considered	N
	8d	Prognostic characteristics (such as staging in oncology) where applicable	N/A
Therapeutic Intervention	9a	Types of intervention (such as pharmacologic, surgical, preventive, self-care)	Y
	9b	Administration of intervention (such as dosage, strength, duration)	N
	9c	Changes in intervention (with rationale)	N
Follow-up and Outcomes	10a	Clinician and patient-assessed outcomes (when appropriate)	Y
	10b	Important follow-up diagnostic and other test results	N
	10c	Intervention adherence and tolerability (How was this assessed?)	N
	10d	Adverse and unanticipated events	N
Discussion	11a	Discussion of the strengths and limitations in your approach to this case	N
	11b	Discussion of the relevant medical literature.	Y
	11c	The rationale for conclusions (including assessment of possible causes)	Y
	11d	The primary "take-away" lessons of this case report	Y
Patient Perspective	12	When appropriate the patient should share their perspective on the treatments they received	N
Informed Consent	13	Did the patient give informed consent? Please provide if requested	Yes ☐ No ☑

Appendix 8: Flow of studies through study post initial literature search



Appendix 9: Flow of studies through study post updated literature search



Appendix 10: Summary of studies included in systematic review entitled "Rehabilitation practices in the treatment of patients with tumours of the posterior fossa

Study	Participants: n, sex, mean age	Study Design	Participant Characteristics	Intervention	Duration of intervention	Outcome Measures
Ada et al, 2009 Australia	One 5 year old female	Single-case design	Had undergone full surgical resection for a low grade, large cerebellar pilocytic astrocytoma 3.5 years previous	Tracking task that required the participant to track the movements of a pseudo-random target on the computer screen using elbow joint flexion and extension	12 Intervention sessions of ten minutes duration	Finger nose test for upper limb dexterity Nine hole peg test. Activity was recorded by speed and smoothness of movement on a 10 point VAS scale
Betker et al, 2006 Canada	Case 1. 20 year old Case 2. 58 year old Case3. 41 year old	Case study	Case 1. Cerebellar tumour excision Case 2. Right CVA Case 3. Closed TBI	Centre of pressure (COP) controlled video game based exercise system No conventional balance rehabilitation	8 x 45 minute sessions over three weeks	Number of falls, range of COP excursion and COP path length
Cremer, 1998 USA	One 15 year old male	Case study	Post Posterior fossa medullablastoma excision with associated chemotherapy and radiotherapy	MDT involvement but specific interventions not documented	Received physiotherapy and occupational therapy input but programme is not outlined	Nil Documented
Gill-body et al, 1997 USA	Case 1. 36 year old female	Case report	Case 1. 7 months post excision of a recurrent cerebellar vermis pilocytic astrocytoma	Customized rehabilitation programmes for both patients that focused on balance, gait and gaze stability exercises to improve functional	Case 1. The patient had a weekly 30-45 minute physiotherapy session with a 30-40 minute HEP completed	Dynamic posturography, dizziness handicap inventory (DHI), gait parameters including velocity, base of support, double

	Case 2. 48 year old male		Case2. Cerebrotendinous xanthamatosis (CX) and diffuse cerebellar atrophy	ability	once daily, 5 days a week for 6 weeks Case2. The patient had weekly 30 minute physiotherapy sessions with a 30 minute HEP completed once daily, 4 times a week for 6 weeks	limb stance time, dynamic gait index
Karakaya et al, 2000 Turkey	7 females and 13 males with posterior fossa tumours 8 females and 12 males with cerebello-pontine angle tumours	Single case design	20 subjects with posterior fossa tumours 20 subjects with cerebello-pontine angle tumours	Frenkel exercise, Proprioceptive neuromuscular facilitation (PNF), Training for dysmetria and disdiadochokinesia, balance, mobility and stairs rehabilitation	Intervention five times weekly for two weeks	Mokken's 4 point rating system to evaluate balance, customized evaluation of gait and limb ataxia

Appendix 11: Initial Ethical Approval

Ethics (Medical Research) Committee - Beaumont Hospital
Notification of ERC/IRB Approval

Principal Investigator: Ms. Kareena Malone (Physio)

Consultant Co-Investigator: Mr. Stephen McNally

REC reference: 12/90

Protocol Title: The impact of surgery on balance and gait parameters in patients with posterior fossa tumours

Ethics Committee Meeting Date: 9th November 2012

Final Approval Date: 20th December 2012

From: Ethics (Medical Research) Committee - Beaumont Hospital, Beaumont, Dublin 9

Documents Reviewed

Document and Date	Date Reviewed	Approved
Application Form, V2	20/12/12	Yes
Research Protocol, no version no.	20/12/12	Yes
Patient Information Leaflet, V2, 12/12	20/12/12	Yes
Patient Consent Form, V1, 10/12	20/12/12	Yes
Letter to Consultant, V1, 10/12	20/12/12	Yes
Letter to GP, V1, 10/12	20/12/12	Yes
Outcome Measures:		
Dizziness Handicap Inventory	20/12/12	Yes
Box Scale for Pain	20/12/12	Yes
Linear Analog Self-Assessment	20/12/12	Yes
Proof of insurance: Royal College of Surgeons in Ireland (renewal: 1/12/12)	20/12/12	Noted
CV: K. Malone, 19/10/12	20/12/12	Noted

Prof. Alice Stanton
ERC/IRB Convenor's Signature
Approval # 1, dated 20/12/12

Appendix 12: Ethical Approval with addition of NHPT

Ethics (Medical Research) Committee - Beaumont Hospital
Notification of ERC/IRB Approval

Principal Investigator: Ms. Kareena Malone (Physio)
Consultant Co-Investigator: Mr. Stephen McNally

REC reference: 12/90

Protocol Title: The impact of surgery on balance and gait parameters in patients with posterior fossa tumours

Ethics Committee Meeting Date: 9th November 2012
Final Approval Date: 20th December 2012

From: Ethics (Medical Research) Committee - Beaumont Hospital, Beaumont, Dublin 9

Documents Reviewed

Document and Date	Date Reviewed	Approved
Application Form,		
V2	20/12/12	Yes
V3	8/2/13*	Yes
Research Protocol, no version no.	20/12/12	Yes
Patient Information Leaflet,		
V2, 12/12	20/12/12	Yes
V3, 01/13	8/2/13*	Yes
Patient Consent Form, V1, 10/12	20/12/12	Yes
Letter to Consultant, V1, 10/12	20/12/12	Yes
Letter to GP, V1, 10/12	20/12/12	Yes
Outcome Measures:		
Dizziness Handicap Inventory	20/12/12	Yes
Box Scale for Pain	20/12/12	Yes
Linear Analog Self-Assessment	20/12/12	Yes
Nine Hole Peg Test	8/2/13*	Yes
Protocol Amendment:		
#1, 31/1/13 (add outcome measure)	8/2/13*	Yes
Proof of insurance:		
Royal College of Surgeons in Ireland		
(renewal: 1/12/12)	20/12/12	Noted
CV: K. Malone, 19/10/12	20/12/12	Noted

Prof. Alice Stanton
ERC/IRB Convenor's Signature
Approval # 2, dated 8th February 2013*

Appendix 13: Patient Information Leaflet

Website: www.beaumont.ie

Ospidéal Beaumont

BEAUMONT HOSPITAL
P. O. Box 1297 Beaumont Road Dublin 9
Telephone: 809 3000 / 837 7755 Facsimile: 837 6982

Patient Information Leaflet

Study title: "The impact of surgery on balance, gait, upper limb dexterity and dizziness in patients with posterior fossa tumours"

Principal investigator's name: Kareena Malone

Principal investigator's title: Senior Physiotherapist in Neurosurgery

Telephone number of principal investigator: (01) 8092526; (01) 8092535

You are being invited to take part in a clinical research study to be carried out at Beaumont Hospital.

Before you decide whether or not you wish to take part, you should read the information provided below carefully and, if you wish, discuss it with your family, friends or GP (doctor). Take time to ask questions – don't feel rushed and don't feel under pressure to make a quick decision.

You should clearly understand the risks and benefits of taking part in this study so that you can make a decision that is right for you. This process is known as 'Informed Consent'.

You don't have to take part in this study. If you decide not to take part it won't affect your future medical or physiotherapy care.

You can change your mind about taking part in the study any time you like. Even if the study has started, you can still opt out. You don't have to give us a reason. If you do opt out, rest assured it won't affect the quality of treatment you get in the future.

Why is this study being done?

Beaumont Hospital is the neurosurgical centre of Ireland and patients are routinely admitted for brain tumour surgery. The posterior portion of the skull houses the brainstem and cerebellum, two portions of the brain involved in the control of balance and walking. These tumours are also associated with causing dizziness. When a patient requires removal of a tumour from one of these portions of the brain, problems with the persons walking and balance can potentially occur.
This study will assess walking, balance and dizziness in the patients before and after surgery to see if they are having any problems with these tasks. It will also allow the testers to see how the different types of tumour and their different locations impact on the patients walking and balance.

Who is organising and funding this study?

Kareena Malone, a Senior Physiotherapist in Beaumont Hospital is carrying out this study. Her supervisors are Mr Stephen McNally, Consultant neurosurgeon in Beaumont Hospital and Dr Rose Galvin and Ms. Dara Meldrum, lecturers in the School of Physiotherapy, Royal College of Surgeons (RCSI), Dublin. The study is part of a Masters Degree through research in RCSI. As requested the following section was deleted from the leaflet (version 2)

Why am I being asked to take part?

You are being asked to take part in this study because you have been admitted to Beaumont Hospital for surgery due to a tumour in the posterior portion of your brain. All patients admitted for this surgery over a one year period will be asked to take part in the study.

How will the study be carried out?

The study will start in December 2012 and will continue until approximately June 2014.
A person who volunteers for the study will have an assessment carried out before surgery, after surgery as an inpatient, at 6 weeks after surgery, on the same day as your clinic review and a telephone follow-up at 6 months. All testing will be carried out in Beaumont Hospital. At the end of the assessment all results will be explained to you.

What will happen to me if I agree to take part?

If you agree to take part in the study you will have an assessment carried out before your surgery in the physiotherapy department of Beaumont Hospital. An appointment will be arranged for a time that suits you. It is best to wear comfortable clothing for the assessments. You will undergo an assessment of your walking, using a marked out walkway that will take 5 minutes. You will also undergo a computerised assessment of your balance using a system called the Equitest which will take a further 15 minutes. A test to look at the control of movement in your hands and arms will be carried out that will take approximately

5 minutes and finally you will complete 2 questionnaires looking at your quality of life and symptoms of dizziness.
After your surgery when you are well enough to recommence physiotherapy, the assessments will be repeated during your stay in hospital and then again at 6 weeks post discharge on the same day as your clinic appointment. The walking and balance tests will be repeated at these times and also the questionnaires.
At 6 months post discharge from Beaumont I will contact you by phone and repeat the 2 questionnaires over the phone.
At the end of the assessments Kareena Malone will explain all the results to you.

What other treatments are available to me?

If you decide not to take part in the study you will receive your medical and physiotherapy care as normal. Refusal to be part of the study will not impact on the care you receive.

What are the benefits?

By taking part in the study you will benefit from detailed assessments, by a physiotherapist before and after surgery. You will receive appropriate advice based on the assessments. Any balance or walking issues you may be having will be picked up by the assessments. The impact of dizziness on your quality of life will also be looked at. By finding these deficits you can be treated more effectively and referred onto the appropriate services, as required

What are the risks?

Although you will be supervised at all times by an experienced physiotherapist, in a safe environment, there is a very small risk that you may sustain a fall as the assessments test your balance. To decrease the risk you can use your normal walking aid as required. You will be closely supervised throughout the testing by the assessor (Kareena Malone).
Neck pain may also occur due to the post-op wound. We will minimise this risk by carefully assessing your pain (Deletion). There is also a small risk of dizziness due to the type of assessments but should you become dizzy I will stop testing. Your level of tiredness will also be monitored throughout testing to prevent you feeling too tired after the tests.

What if something goes wrong when I'm taking part in this study?

If you experience any problems as a result of participating in this study Kareena Malone will be responsible for dealing with these problems and will discuss them with your consultant and his team if required.

Will it cost me anything to take part?

There is a time commitment required to complete the assessments that are part of this study. However, these assessments will be arranged during your stay in hospital or during your follow up clinic visit.

Is the study confidential?

The main investigator (Kareena Malone) will look at your medical chart and online scan to gather the required information. Your GP and consultant will be informed of your taking part in the study. All of your information will be coded for protection. Your coded information will be saved on encrypted USB keys for five years after which time it will be destroyed according to the Beaumont policy

Where can I get further information?

If you have any further questions about the study or if you want to opt out of the study, you can rest assured it won't affect the quality of treatment you get in the future.
If you need any further information now or at any time in the future, please contact:

Name: Kareena Malone
Address: Physiotherapy Department, Beaumont Hospital, Beaumont Road, Dublin 9

Phone No: (01) 8092526; (01) 8092535

Appendix 14: Participant Consent Form

Website: www.beaumont.ie

Ospidéal Beaumont

BEAUMONT HOSPITAL
P. O. Box 1297 Beaumont Road Dublin 9
Telephone: 809 3000 / 837 7755 Facsimile: 837 6982

Patient Consent Form

Study title: **"The Impact of surgery on balance, gait, upper limb dexterity and dizziness in patients with posterior fossa tumours"**

I have read and understood the **Information Leaflet** about this research project. The information has been fully explained to me and I have been able to ask questions, all of which have been answered to my satisfaction.	**Yes** ☐	**No** ☐
I understand that I don't have to take part in this study and that I can opt out at any time. I understand that I don't have to give a reason for opting out and I understand that opting out won't affect my future physiotherapy treatment or medical care.	**Yes** ☐	**No** ☐
I am aware of the potential risks of this research study.	**Yes** ☐	**No** ☐
I give permission for my GP to be informed of my involvement in this research study	**Yes** ☐	**No** ☐
I give permission for my Consultant to be informed of my involvement in this research study	**Yes** ☐	**No** ☐
I give permission for researchers to look at my medical records to get information. I have been assured that information about me will be kept private and confidential.	**Yes** ☐	**No** ☐
I have been given a copy of the Information Leaflet and this completed consent form for my records.	**Yes** ☐	**No** ☐
I give permission to be contacted by telephone post discharge	**Yes** ☐	**No** ☐
Storage and future use of information: I give my permission for information collected about me to be stored or electronically processed for the purpose of scientific research and to be used in <u>related studies or other studies in the future</u> but only if the research is approved by a Research Ethics Committee.	**Yes** ☐	**No** ☐

Patient Name (Block Capitals)	Patient Signature	Date

To be completed by the Principal Investigator or nominee.

I, the undersigned, have taken the time to fully explain to the above patient the nature and purpose of this study in a way that they could understand. I have explained the risks involved as well as the possible benefits. I have invited them to ask questions on any aspect of the study that concerned them.

--Name (Block Capitals)	Qualifications	Signature	Date

3 copies to be made: 1 for patient, 1 for PI and 1 for hospital records.

Appendix 15: Consultant letter of participant involvement in study

Website: www.beaumont.ie

Ospidéal Beaumont

BEAUMONT HOSPITAL
P. O. Box 1297 Beaumont Road Dublin 9
Telephone: 809 3000 / 837 7755 Facsimile: 837 6982

Physiotherapy Department,
Beaumont Hospital,
Beaumont Road,
Dublin 9.

Xx/xx/xxxx

Re: **"The impact of surgery on balance, gait, upper limb dexterity and dizziness in patients with posterior fossa tumours"**

Dear Mr_____,

I am writing in relation to a study that I am conducting in Beaumont Hospital physiotherapy department as part of an MSc by research, investigating the impact on balance and gait post posterior fossa tumour surgery. _____ was recruited to the study during their inpatient stay in Beaumont Hospital.

The project is being supervised by Mr. Stephen McNally, Consultant Neurosurgeon, Beaumont Hospital, Dr. Rose Galvin, School of Physiotherapy, Royal College of Surgeons and Ms. Dara Meldrum, School of physiotherapy, Royal College of Surgeons.

Participation in the study involves a pre-operative assessment that looks at balance, gait and dizziness. Post operatively the assessments are repeated during the inpatient stay, at the 6 week neurosurgical clinic review and a phone follow-up at 6 months. All objective assessments will be completed by the principal investigator, Kareena Malone, in the physiotherapy department of Beaumont Hospital.

If you have any queries please don't hesitate to contact me to discuss them further. I can be contacted on (01) 8092535

Yours sincerely,

_____

Kareena Malone, Senior Physiotherapist in Neurosurgery, Beaumont Hospital

Appendix 16: GP information letter

Website: www.beaumont.ie

Ospidéal Beaumont

BEAUMONT HOSPITAL
P. O. Box 1297 Beaumont Road Dublin 9
Telephone: 809 3000 / 837 7755 Facsimile: 837 6982

Physiotherapy Department,
Beaumont Hospital,
Beaumont Road,
Dublin 9.

Xx/xx/xxxx

Re: **"The impact of surgery on balance, gait, upper limb dexterity and dizziness in patients with posterior fossa tumours"**

Dear Dr_____

I am writing in relation to a study that I am conducting in Beaumont Hospital physiotherapy department investigating the impact on balance and gait post posterior fossa tumour surgery. _____ was recruited to the study during their inpatient stay in Beaumont Hospital.

The project is being supervised by Mr. Stephen McNally, Consultant Neurosurgeon, Beaumont Hospital and Dr. Rose Galvin and Dara Meldrum based in the School of Physiotherapy, Royal College of Surgeons.

Participation in the study involves a pre-operative assessment that looks at balance, gait and dizziness. Post operatively the assessments are repeated during the inpatient stay, at the 6 week neurosurgical clinic review and a phone follow-up at 6 months. All objective assessments will be completed by the principal investigator, Kareena Malone, in the physiotherapy department of Beaumont Hospital.

If you have any queries please don't hesitate to contact me to discuss them further. I can be contacted on (01) 8092535

Yours sincerely,

Kareena Malone, Senior Physiotherapist in Neurosurgery, Beaumont Hospital

Appendix 17: Data collection sheet

Data Collection Sheet

Subject Reference Number

Patient Name	
Sex	
Age	
Height	
Weight	
MRI/CT	MRI CT
Location of SOL	
Size of SOL	
Histology	
Mass Effect	
Midline Shift	
Surgical procedure	
Total Excision	
Subtotal Excision	
For Chemotherapy	
For Radiotherapy	
Headache	
Nausea	
Vomitting	
Visual Deficit	
GCS on admission	
Dizziness	
Hydrocephalus	
Vertigo	
Tinnitus	
Oscillopsia	
Mobility Aid	
Days post op for initial assessment	
Days post op for clinic assessment	
Number of inpatient days	
ITU Admission	

Appendix 18: Testing protocol at varying time-points

Outcome Measure	T1	T2	T3	T4
CDP	√	√	√	
10m Walks	√	√	√	
NHPT	√	√	√	
DHI	√	√	√	√
LASA	√			√
Box Scale		√	√	√
Demographics	√			
Tumour Data	√	√		
Length of Stay			√	

Appendix 19: Checklist for T1

Testing Checklist T1

Written and Verbal consent Obtained	
Copy of written consent to participant	
Copy of written consent placed in Med chart	
T1 assessment time scheduled	
Testing procedure explained to participant	
10m walk tests completed	
LASA Completed	
NHPT Completed	
DHI Completed	
Equitest Completed	
Tumour Parameters obtained	

Appendix 20: Checklist for T2

Testing Checklist T2

Physiotherapy referral received from team	
Postoperative tumour data obtained	
T2 assessment time scheduled	
Testing procedure explained to participant	
10m walk Completed	
LASA Completed	
Box Pain completed	
NHPT Completed	
DHI Completed	
Equitest Completed	
Confirm phone contact will be made re clinic appointment	
Liase with secretaries re clinic appointment	
Refer to CPT if required	

Appendix 21: Checklist for T3

Testing Checklist T3

Phone patient on day of clinic to ensure attendance	
Testing procedure explained to participant	
10m walk Completed	
Box Pain completed	
NHPT Completed	
DHI Completed	
Equitest Completed	
Refer to CPT if required	
Advise re phone contact at 6 months	
Forward letter to the GP	
Forward letter to consultant	
Insert date in diary for phone followup	

Appendix 22: Checklist for T4

Testing Checklist T4

DHI completed	
LASA Completed	
Box scale completed	
Refer to CPT if required	

Appendix 23: 10m Walk test protocol

10m Walking Test Protocol

The testing protocol used for the 10m walk tests was that outlined by Peters et al, 2013.

Walking speed was assessed at participants' self-selected walking speed, fastest walking speed and self -selected walking speed with horizontal head turns using the 10-Meter Walk Test.

Distances were provided at the beginning and end of the timed walkway (5m) to allow participants space to accelerate/decelerate outside the data collection area to help reduce gait variability.

Each participant completed 3 consecutive trials for each walking test, for a total of 9 walking trials.

Order of administration of the 3 different walking conditions was self-selected, fast and self-selected with horizontal head turns, to allow participants an opportunity to familiarise themselves with the task, starting with those considered the easier tasks.

Participants were instructed to “walk at your comfortable, normal pace” until they reached the end of the marked path for the self-selected speed.

Participants were instructed to “walk as fast as you can but ensure you feel steady and safe” until they reached the end of the marked path for the fastest walking speed.

Participants were instructed to “walk at your comfortable speed and turn your head from side to side, as fast as you can while keeping your balance” until they reached the end of the marked path for the walking trials with horizontal head turns.

The PI measured walking time with a stopwatch, starting the stopwatch as soon as the participant's lead leg (or assistive device) crossed the first marker and stopping it when the participant's lead leg (or assistive device) crossed the second marker.

The PI performed all stopwatch measurements to prevent introducing inter-rater variability.

Participants were provided rest breaks as needed throughout the testing session.

Averages were obtained for the three trials, for each condition tested

Appendix 24: NHPT testing protocol

Nine Hole Peg Test Protocol

The protocol was implemented based on the original protocol outlined by Mathiowetz et al, 1985.

The NHPT test consisted of a plastic console with a shallow round dish to contain the pegs on one end of the console and the nine-hole peg-board on the opposite end.

Each participant was asked to centre the pegboard directly in front of him or her, oriented such that the shallow dish was on the participant's dominant hand side and the peg holes on the non-dominant side.

The participant was instructed to "place each of the nine pegs in the nine holes and once all nine pegs are in the holes, take them out, one at the time".

Participants were given the opportunity for a brief practice test prior to the actual test and were then tested using their dominant hand first, followed by their non-dominant hand.

The tests were timed, with a stopwatch, from the moment the participant touched the first peg until the moment the last peg hit the dish.

The test was then repeated for the non-dominant hand using the same testing method, with the pegboard rotated such that the dish was in front of the non-dominant hand.

All participants were tested using this procedure.

In the event that the participant dropped a peg or the trial was interrupted in any way, the PI cued the participant to stop and a new trial was initiated.

Appendix 25: DHI

DIZZINESS HANDICAP INVENTORY

Name: _____ **Date:** _____

Part I

Instructions: The purpose of this scale is to identify difficulties that you may be experiencing because of your dizziness or unsteadiness. Please indicate answer by circling "yes or "no" or "sometimes" for each question. Answer each question as it pertains to your dizziness or unsteadiness problem only.

P1. Does looking up increase your problem?	Yes	No	Sometimes
E2. Because of your problem, do you feel frustrated?	Yes	No	Sometimes
F3. Because of your problem, do you restrict your travel for business or recreation?	Yes	No	Sometimes
P4. Does walking down the aisle of a supermarket increase your problem?	Yes	No	Sometimes
F5. Because of your problem, do you have difficulty getting into or out of bed?	Yes	No	Sometimes
F6. Does your problem significantly restrict your participation in social activities such As going out to dinner, going to the movies, dancing, or to parties?	Yes	No	Sometimes
F7. Because of your problem, do you have difficulty reading?	Yes	No	Sometimes
P8. Does performing more ambitious activities like sports, dancing, household chores Such as sweeping or putting away dishes increase your problem?	Yes	No	Sometimes
E9. Because of your problem, are you afraid to leave your home without having someone accompany you?	Yes	No	Sometimes
E10. Because of your problem, have you been embarrassed in front of others	Yes	No	Sometimes
P11. Do quick movements of your head increase your problem?	Yes	No	Sometimes
F12. Because of your problem, do you avoid heights?	Yes	No	Sometimes
P13. Does turning over in bed increase your problem?	Yes	No	Sometimes
F14. Because of your problem, is it difficult for you to do strenuous housework or yard work?	Yes	No	Sometimes
E15. Because of your problem, are you afraid people might think you are intoxicated?	Yes	No	Sometimes
F16. Because of your problem, is it difficult for you to go for a walk by yourself?	Yes	No	Sometimes
P17. Does walking down a sidewalk increase your problem?	Yes	No	Sometimes
E18. Because of your problem, is it difficult for you to concentrate?	Yes	No	Sometimes

F19. Because of your problem, is it difficult for you walk around the house in the dark?	Yes	No	Sometimes
E20. Because of your problem, are you afraid to stay home alone?	Yes	No	Sometimes
E21. Because of your problem, do you feel handicapped?	Yes	No	Sometimes
E22. Has your problem placed stress on your relationships with members of your family or friends?	Yes	No	Sometimes
E23. Because of your problem, are you depressed?	Yes	No	Sometimes
F24. Does your problem interfere with your job or household responsibilities?	Yes	No	Sometimes
P25. Does bending over increase your problem?	Yes	No	Sometimes

Part II
Instructions: Put a check in the box that best describes you.

☐	**Negligible symptoms (0)**
☐	**Bothersome symptoms (1)**
☐	**Performs usual work duties but symptoms interfere with outside activities (2)**
☐	**Symptoms disrupt performance of both usual work duties and outside activities (3)**
☐	**Currently on medical leave or had to change jobs because of symptoms (4)**
☐	**Unable to work for over one year or established permanent disability with compensation payments (5)**

STOP HERE

	Yes		Sometimes		No	
P(7)	_____x4=____	+	_____x2=____	+	_____x0=____	**Physical Items_____ (28)**
E(9)	_____x4=____	+	_____x2=____	+	_____x0=____	**Emotional Items_____ (36)**
F(9)	_____x4=____	+	_____x2=____	+	_____x0=____	**Functional Items_____ (36)**

TOTAL_____
(max 100 pts)

Appendix 26: Box scale for pain

Box Scale for Pain

Each number (e.g. 0–10) is written in a box and patients are asked:
"If a zero (0) means 'no pain' and a ten (10) means 'pain as bad as it could be', on this scale of 0–10, what is your level of pain? Put an "X" through that number."[13]

0	1	2	3	4	5	6	7	8	9	10

Appendix 27: Linear Analogue Scale Assessment (LASA)

Linear Analogue self-assessment

Adapted from the protocol used by Locke et al, 2007

Directions: Please circle the number (0-10) best reflecting your response to the following that best describes your feelings during the past week, including today.

1. How would you rate your physical well-being over the past week?
This question refers to such things as fatigue, activity, etc.

0 1 2 3 4 5 6 7 8 9 10
As bad as it can be — As good as it can be

2. How would you rate your emotional well-being over the past week?
This question refers to such things as depression, anxiety, stress, etc.

0 1 2 3 4 5 6 7 8 9 10
As bad as it can be — As good as it can be

3. How would you rate your spiritual well-being over the past week?
This question refers to such things as a sense of meaning and purpose, relationship with God, etc.

0 1 2 3 4 5 6 7 8 9 10
As bad as it can be — As good as it can be

4. How would you rate your intellectual well-being over the past week?
This question refers to such things as the ability to think clearly, to concentrate, to remember, etc.

0 1 2 3 4 5 6 7 8 9 10
As bad as it can be — As good as it can be

5. How would you rate your overall well-being over the past week?

0 1 2 3 4 5 6 7 8 9 10

As bad as it can be — As good as it can be

Appendix 28: Data collection spread-sheet

ID	Sex	Age	Height	MRI	CT	SOL Location	SOL Size_cm
PT001	2	59	171	1	1	4	3.5
PT002	2	34	159	1	1	2	3.4
PT003	1	56	174	1	1	4	3.7
PT004	1	40	173	1	1	2	2.5
PT005	2	69	164	1	1	4	4
PT006	1	21	171	1	1	2	4.3
PT007	2	44	170	1	1	4	3.2
PT008	1	49	177	1	2	4	2.5
PT009	2	39	160	1	1	3	2.5
PT010	2	62	159	1	1	3	3
PT011	1	77	175	1	1	4	4
PT012	2	51	160	1	1	4	4.5
PT013	2	34	160	1	1	4	3.9

Intra-axial	Extra-axial	Midline Shift	Mass Effect	Histology	WHO Grade	No. of Surgeries
1	2	2	1	1	4	2
1	2	2	2	2	2	1
1	2	2	1	1	4	1
1	2	2	2	3	2	3
2	1	2	1	4	1	1
1	2	2	2	6	1	5
2	1	1	1	4	1	1
1	2	2	2	1	4	1
1	2	2	1	1	4	1
1	2	2	2	1	4	1
1	2	2	1	1	4	1
1	2	2	2	5	1	2
1	2	1	1	1	4	1

Exposure	Total Ex	Subtotal Ex	Chemo	RTX	Headache	Nausea	Vomiting
1	1	2	1	1	2	2	2
1	1	2	2	2	2	1	2
2	1	2	2	1	1	1	2
2	1	2	2	2	1	1	1
1	2	1	2	2	2	2	2
1	1	2	2	2	1	2	2
1	2	1	2	2	1	2	2
1	1	2	1	1	1	2	2
1	1	2	1	1	1	1	1
1	2	1	1	1	2	1	1
1	2	1	2	1	1	1	1
1	1	2	2	2	1	2	2
1	1	2	2	1	1	1	1

Visual Disturbance	Adm_GCS	Dizziness	Hydrocephalus	EVD	Shunt	Haemorrhage	Vertigo
2	1	2	1	2	2	1	2
2	1	1	1	1	2	1	1
2	1	1	2	2	2	2	2
2	1	1	2	1	2	1	1
2	1	2	2	2	2	2	2
1	1	1	1	1	1	1	2
1	1	2	2	2	2	2	2
1	1	2	1	2	2	2	2
1	1	2	1	2	2	2	2
1	1	1	2	2	2	2	2
2	1	1	1	2	2	2	2
2	1	1	1	1	2	2	2
2	1	2	1	2	2	2	2

Tinnitus	Oscillopsia	Mobility aid	Aid type	ITU admin	DaysITU	Secondary	PrimaryLOC
2	2	2	5	1	3	1	1
1	2	2	5	1	1	2	6
2	2	2	5	2	0	1	4
2	2	2	5	1	14	2	6
2	2	2	5	2	0	2	6
2	2	2	5	1	18	2	6
2	2	2	5	2	0	2	6
2	2	2	5	2	0	1	5
2	2	2	5	2	0	1	5
2	2	1	2	2	0	1	2
2	2	2	5	2	0	1	5
2	2	2	5	2	0	2	6
2	2	2	5	2	0	1	1

Mortality T1	Mortality T2	Mortality T3	Mortality T4	Morbidity T1	Morbidity T2	Morbidity T3	Morbidity T4
2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2
2	2	2	1	2	1	1	3
2	2	2	2	2	2	2	2
2	2	2	2	2	1	1	1
2	2	2	2	2	2	2	2
2	2	2	1	2	2	2	3
2	2	2	1	2	2	2	3
2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	1
2	2	2	2	2	2	2	2
2	2	2	2	2	2	2	2

Inpt Days	ET_TP1_Comp	ET_TP2_Comp	ET_TP3_Comp	ET_Cond5_T1_Av	NoFalls_Cond5_T1
15	44	49	74	0	3
36	77	57	79	64	0
7	67	67		49	0
41	75			64	0
8	71	62	68	45	0
81	70			38	1
7	61		77	0	3
5	41		29	17	2
6	47	64		0	3
12	42	61	52	0	3
15	34	50		0	3
16	51	56	81	0	3
8	83	86	85	59	0

ET_Cond5_T2_Av	NoFalls_Cond5_T2	ET_Cond5_T3_Av	NoFalls_Cond5_T3	ET_Cond6_T1_Av
22	1	63	0	16
0	3	65	0	58
24	1			42
				54
41	0	31	1	46
				50
		56	0	64
		0	3	0
37	1			18
0	3	0	3	0
9	2			0
0	3	70	0	34
47	0	71	0	82

Gait Speed_T1_Preferred m/sec	Gait Speed_T2_Preferred m/sec	Gait Speed_T3_Preferred m/sec
1.54	0.72	1.38
1.18	0.31	1.07
1.44	1.58	
1.55		
1.24	1.11	1.38
1.43		
1.66		1.56
0.87		0.84
1.17	0.46	
1.03	0.93	1.37
0.91	0.98	
1.6	1.36	1.45
1.41	1.43	1.38

Gait Speed_T1_Max m/sec	Gait Speed_T2_Max m/sec	Gait Speed_T3_Max m/sec
1.93	1.09	1.84
1.53	0.4	1.09
1.7	1.74	
2.06		
1.53	1.3	1.62
2.7		
1.9		1.75
1.25		1.11
1.5	0.71	
1.28	1.18	1.53
1.4	1.34	
1.7	1.5	1.64
1.84	1.48	1.66

Gait Speed_T1_HT m/sec	Gait Speed_T2_HT m/sec	Gait Speed_T3_HT m/sec
1.62	0.86	1.4
1.32	0.26	0.59
1.5	1.5	
1.64		
1.32	1.19	1.38
1.57		
1.49		1.7
1.04		0
0.71	0.46	
0.88	0.86	1.18
1.09	1.1	
1.41	1.06	1.34
1.7	1.22	1.3

DHI_Comp_1	DHI_Comp_2	DHI_Comp_3	DHI_Comp_4	LASA_1_1 Overall QOL	LASA_2_1 Mental
6	40	20	20	5	8
6	72	64	56	9	10
2	2		58	8	8
32				7	5
0	4	0	0	10	10
0					
2		0	0	10	10
68		58		4	5
32	66			2	4
50	64	52	42	8	8
14	36			8	8
50	0	0	0	7	7
14	6	0	0	10	10

LASA_3-1 Physical	LASA_4_1 Emotional	LASA_6_1 Spiritual	LASA_1_4 Overall QOL	LASA_2_4 Mental
8	8	6	7	7
10	9	10	5	6
5	8	8	4	7
6	7	10		
10	8	10	7	10
10	7	10	10	8
3	5	2		
10	4	10		
8	8	9	6	5
9	7	8		
6	7	7	10	10

	10	10	10	8		10
LASA_3_4 Physical	LASA_4_4 Emotional	LASA_6_4 Spiritual	Box_2	Box_3	Box_4	HandDom
7	7	7	3	0	0	1
4	6	8	1	2	0	1
3	7	6	3		1	2
						1
7	6	7	5	0	3	1
						2
10	8	10		0	0	1
			8	0		1
			3			1
6	6	10	0	0	0	1
			6			1
10	10	10	0	0	0	1
8	8	8	2	0	0	1

NHPT_1_R_secs	NHPT_1_L_secs	NHPT_2_R_secs	NHPT_2_L_secs	NHPT_3_R_secs	NHPT_3_L_secs	D/c Destination
18.95	29.08	24.53	34.69	14.94	36.19	1
22.09	20.17	25.71	27.16	19.52	20.38	1
26.63	28.53	25.12	28.14			1
20.87	21.84					3
20.59	20	22.69	21.83	21.81	19.78	1
17.75	17.64					3
16.51	16.63			17.34	18.19	1
68	97			59.26	52.45	3
21.13	25.2	23.5	25.5			3
28.8	23.56	30.88	32.25	24.77	22.76	1
22.4	27.2	22.84	21.72			1
17.46	20.3	18.87	18.23	16.59	16.31	1
15.33	20.09	16.09	19.64	20.18	21.2	1

Appendix 29: Data Codebook

Variable Name	Response Options	Codes	Units
Age			
Sex	Male	Male = 1	
	Female	Female = 2	
Height			cm
CT	Yes	Yes = 1	
	No	No = 2	
MRI	Yes	Yes = 1	
	No	No = 2	
Histology	Mets	Mets = 1	
	Ependymoma	Ependymoma = 2	
	Atypical choroid plexus papilloma	Atypical Choroid Plexus Papilloma = 3	
	Meningioma	Meningioma = 4	
	Haemangioblastoma	Haemangioblastoma = 5	
	Pilocytic Astrocytoma	Pilocytic Astrocytoma = 6	
Who Classification	WHO 1	WHO 1 = 1	
	WHO 2	WHO 2 =2	
	WHO 3	WHO 3 = 3	
	WHO 4	WHO 4 = 4	
Number of surgeries	1 Surgery	1 Surgery = 1	
	2 Surgeries	2 Surgeries = 2	
	3 Surgeries	3 Surgeries = 3	
	4 Surgeries	4 Surgeries = 4	
	5 Surgeries	5 Surgeries = 5	
Surgery to expose Tumour	Craniectomy	Craniectomy = 1	
	Craniotomy	Craniotomy = 2	
Total Excision	Yes	Yes = 1	
	No	No = 2	
Subtotal Excision	Yes	Yes = 1	
	No	No = 2	
Supplementary Surgery	Haematoma Evacuation	Haematoma Evacuation = 1	
	Shunt Insertion	Shunt Insertion = 2	
	EVD insertion	EVD = 3	
	Nil	Nil = 4	
Chemotherapy	Yes	Yes = 1	
	No	No = 2	
Radiotherapy	Yes	Yes = 1	
	No	No = 2	
Headache	Yes	Yes = 1	
	No	No = 2	
Nausea	Yes	Yes = 1	
	No	No = 2	
Vomiting	Yes	Yes = 1	

	No	No = 2
Visual Disturbance	Yes	Yes = 1
	No	No = 2
GCS	GCS 15	GCS 15 = 1
	GCS 14	GCS 14 = 2
	GCS 13	GCS 13 = 3
	GCS 12	GCS 12 = 4
	GCS 11	GCS 11 = 5
	GCS 10	GCS 10 = 6
	GCS 9	GCS 9 = 7
	GCS 8	GCS 8 = 8
	GCS 7	GCS 7 = 9
	GCS 6	GCS 6 = 10
	GCS 5	GCS 5 = 11
	GCS 4	GCS 4 = 12
	GCS 3	GCS 3 = 13
Dizziness	Yes	Yes = 1
	No	No = 2
Hydrocephalus	Yes	Yes = 1
	No	No = 2
EVD	Yes	Yes = 1
	No	No = 2
Shunt Insertion	Yes	Yes = 1
	No	No = 2
Haemorrhage	Yes	Yes = 1
	No	No = 2
Vertigo	Yes	Yes = 1
	No	No = 2
Tinnitus	Yes	Yes = 1
	No	No = 2
Oscillopsia	Yes	Yes = 1
	No	No = 2
Mobility Aid	Yes	Yes = 1
	No	No = 2
Type of mobility aid	Walking stick	Walking stick = 1
	Zimmer frame	Zimmer frame = 2
	1 crutch	1 crutch = 3
	2 crutches	2 crutches = 4
	Independent	Independent = 5
Number of days to assessment		
ITU admission	Yes	Yes = 1
	No	No = 2
Secondary lesion	Yes	Yes = 1
	No	No = 2
Primary lesion	Breast	Breast = 1
	Ovary	Ovary = 2

	Liver	Liver = 3
	Colon	Colon = 4
	Lung	Lung = 5
	Not applicable	NA = 6
Dizziness	Yes	Yes = 1
	No	No = 2
	Sometimes	Sometimes = 3
Midline Shift	Yes	Yes = 1
	No	No = 2
Mass Effect	Yes	Yes = 1
	No	No = 2
Location of Tumour	Brainstem	Brainstem = 1
	4th Ventricle	4th Ventricle =2
	Cerebellar vermis	Cerebellar Vermis = 3
	Cerebellar Cortex	Cerebellar Cortex = 4
Hand Dominance	Right	Right = 1
	Left	Left = 2
Status at 6 months	Independent	Independent = 1
	Mobile with an aid	Aid = 2
	Mobile with assistance of one person	One person = 3
	Mobile with assistance of two persons	Two people = 4
	Wheelchair Mobiliser	Wheelchair = 5
	Confined to bed	Bed = 6
	RIP	RIP = 7
Current Chemo	Yes	Yes = 1
	No	No = 2
Current Rtx	Yes	Yes = 1
	No	No = 2
GCS	GCS 15	GCS 15 = 1
	GCS 14	GCS 14 = 2
	GCS 13	GCS 13 = 3
	GCS 12	GCS 12 = 4
	GCS 11	GCS 11 = 5
	GCS 10	GCS 10 = 6
	GCS 9	GCS 9 = 7
	GCS 8	GCS 8 = 8
	GCS 7	GCS 7 = 9
	GCS 6	GCS 6 = 10
	GCS 5	GCS 5 = 11
	GCS 4	GCS 4 = 12
	GCS 3	GCS 3 = 13
	RIP	RIP = 14
D/c destination	Home	Home = 1
	Convalescence	Convalescence = 2
	Referring Hospital	Referring Hospital = 3
Mortality	Dead	Dead = 1

	Alive	Alive = 2
Significant Morbidity	Significant Morbidity	Yes = 1
	No significant Morbidity	No = 2
	Dead	Dead =3

Appendix 30: STATA Output

```
. tab Sex
```

Sex	Freq.	Percent	Cum.
1	5	38.46	38.46
2	8	61.54	100.00
Total	13	100.00	

Gender (Male= 1; Female = 2)

```
. summarize Age
```

Variable	Obs	Mean	Std. Dev.	Min	Max
Age	13	48.84615	15.66762	21	77

Age

Adm_GCS	Freq.	Percent	Cum.
1	13	100.00	100.00
Total	13	100.00	

GCS at admission

GCS	GCS 15	GCS 15 = 1
	GCS 14	GCS 14 = 2
	GCS 13	GCS 13 = 3
	GCS 12	GCS 12 = 4
	GCS 11	GCS 11 = 5
	GCS 10	GCS 10 = 6
	GCS 9	GCS 9 = 7
	GCS 8	GCS 8 = 8
	GCS 7	GCS 7 = 9
	GCS 6	GCS 6 = 10
	GCS 5	GCS 5 = 11
	GCS 4	GCS 4 = 12
	GCS 3	GCS 3 = 13

Coding structure used to code GCS, indicating all participants at recruitment had GCS 15. Taken from Excel codebook

Mobility aid	Freq.	Percent	Cum.
1	1	7.69	7.69
2	12	92.31	100.00
Total	13	100.00	

Use of Mobility Aid (Yes = 1; No = 2)

Aid type	Freq.	Percent	Cum.
2	1	7.69	7.69
5	12	92.31	100.00
Total	13	100.00	

Mobility Aid type

Type of mobility aid	Walking stick	Walking stick = 1
	Zimmer frame	Zimmer frame = 2
	1 crutch	1 crutch = 3
	2 crutches	2 crutches = 4
	Independent	Independent = 5

Coding structure used to code for mobility aid use pre admission, indicating one participant used a zimmer-frame pre admission, 12 participants mobilised independently. Taken from Excel codebook

```
. tab HandDom
```

HandDom	Freq.	Percent	Cum.
1	11	84.62	84.62
2	2	15.38	100.00
Total	13	100.00	

Hand Dominance (Right = 1; Left = 2)

```
. summarize SOLSize_cm
```

Variable	Obs	Mean	Std. Dev.	Min	Max
SOLSize_cm	13	3.461538	.687433	2.5	4.5

Tumour size (cm)

```
. tab SOLLocation
```

SOL Location	Freq.	Percent	Cum.
2	3	23.08	23.08
3	2	15.38	38.46
4	8	61.54	100.00
Total	13	100.00	

.

Tumour Location

Location of Tumour	Brainstem	Brainstem = 1
	4th Ventricle	4th Ventricle =2
	Cerebellar vermis	Cerebellar Vermis = 3
	Cerebellar Cortex	Cerebellar Cortex = 4

Coding structure for location of brain tumour within Posterior fossa. Taken from Excel codebook

```
. tab Intraaxial
```

Intra-axial	Freq.	Percent	Cum.
1	11	84.62	84.62
2	2	15.38	100.00
Total	13	100.00	

Intra-axial lesion (Yes = 1; No = 2)

```
. tab Extraaxial
```

Extra-axial	Freq.	Percent	Cum.
1	2	15.38	15.38
2	11	84.62	100.00
Total	13	100.00	

Extra-axial lesion (Yes = 1; No = 2)

```
. tab Histology
```

Histology	Freq.	Percent	Cum.
1	7	53.85	53.85
2	1	7.69	61.54
3	1	7.69	69.23
4	2	15.38	84.62
5	1	7.69	92.31
6	1	7.69	100.00
Total	13	100.00	

Histology

Histology	Mets	Mets = 1
	Ependymoma	Ependymoma = 2
	Atypical chorioid plexus papilloma	Atypical Choroid Plexus Papilloma = 3
	Meningioma	Meningioma = 4
	Haemangioblastoma	Haemangioblastoma = 5
	Pilocytic Astrocytoma	Pilocytic Astrocytoma = 6

Coding structure used for tumour histology. Taken from Excel codebook

```
. tab WHOGrade
```

WHO Grade	Freq.	Percent	Cum.
1	4	30.77	30.77
2	2	15.38	46.15
4	7	53.85	100.00
Total	13	100.00	

WHO classification

Who Classification	WHO 1	WHO 1 = 1
	WHO 2	WHO 2 =2
	WHO 3	WHO 3 = 3
	WHO 4	WHO 4 = 4

Coding structure used for WHO tumour classification. Taken from Excel codebook

```
. tab Secondary
```

Secondary	Freq.	Percent	Cum.
1	7	53.85	53.85
2	6	46.15	100.00
Total	13	100.00	

Secondary tumour (Yes = 1; No = 2)

```
tab Histology PrimaryLOC
```

	PrimaryLOC					
Histology	1	2	4	5	6	Total
1	2	1	1	3	0	7

Location of Primary lesions

Primary lesion	Breast	Breast = 1
	Ovary	Ovary = 2
	Liver	Liver = 3
	Colon	Colon = 4
	Lung	Lung = 5
	Not applicable	NA = 6

Location of primary lesion in participants diagnosed with a secondary lesion. Data from Excel codebook

```
. tab Chemo
```

Chemo	Freq.	Percent	Cum.
1	4	30.77	30.77
2	9	69.23	100.00
Total	13	100.00	

Requiring post-operative chemotherapy (Yes = 1; No = 2)

```
. tab RTX
```

RTX	Freq.	Percent	Cum.
1	7	53.85	53.85
2	6	46.15	100.00
Total	13	100.00	

Requiring post-operative radiotherapy (Yes = 1; No = 2)

```
. tab MRI
```

MRI	Freq.	Percent	Cum.
1	13	100.00	100.00
Total	13	100.00	

MRI

```
. tab CT
```

CT	Freq.	Percent	Cum.
1	12	92.31	92.31
2	1	7.69	100.00
Total	13	100.00	

CT (Yes=1; No=2)

```
. tab NoofSugeries
```

No. of Sugeries	Freq.	Percent	Cum.
1	9	69.23	69.23
2	2	15.38	84.62
3	1	7.69	92.31
5	1	7.69	100.00
Total	13	100.00	

Number of surgical procedures

Number of surgeries	1 Surgery	1 Surgery = 1
	2 Surgeries	2 Surgeries = 2
	3 Surgeries	3 Surgeries = 3
	4 Surgeries	4 Surgeries = 4
	5 Surgeries	5 Surgeries = 5

Number of surgical interventions participants underwent while a neurosurgical inpatient. Data from Excel codebook

```
. tab Exposure
```

Exposure	Freq.	Percent	Cum.
1	11	84.62	84.62
2	2	15.38	100.00
Total	13	100.00	

Surgical Exposure technique

Surgery to expose Tumour	Craniectomy	Craniectomy = 1
	Craniotomy	Craniotomy = 2

Coding structure for surgical technique used to expose tumour. Data from Excel codebook

```
. tab TotalEx
```

Total Ex	Freq.	Percent	Cum.
1	9	69.23	69.23
2	4	30.77	100.00
Total	13	100.00	

Total Excision (Yes = 1; No = 2)

```
. tab SubtotalEx
```

Subtotal Ex	Freq.	Percent	Cum.
1	4	30.77	30.77
2	9	69.23	100.00
Total	13	100.00	

Subtotal Excision (Yes = 1; No = 2)

```
. tab MassEffect
```

Mass Effect	Freq.	Percent	Cum.
1	7	53.85	53.85
2	6	46.15	100.00
Total	13	100.00	

Presence of mass effect on scan (Yes = 1; No = 2)

```
. tab MidlineShift
```

Midline Shift	Freq.	Percent	Cum.
1	2	15.38	15.38
2	11	84.62	100.00
Total	13	100.00	

Presence of midline shift on scan (Yes = 1; No = 2)

```
. tab Hydrocephalus
```

Hydrocephalus	Freq.	Percent	Cum.
1	8	61.54	61.54
2	5	38.46	100.00
Total	13	100.00	

Presence of hydrocephalus on scan (Yes = 1; No = 2)

```
. tab EVD
```

EVD	Freq.	Percent	Cum.
1	4	30.77	30.77
2	9	69.23	100.00
Total	13	100.00	

Requiring insertion of an EVD (Yes = 1; No = 2)

```
. tab Shunt
```

Shunt	Freq.	Percent	Cum.
1	1	7.69	7.69
2	12	92.31	100.00
Total	13	100.00	

Requiring insertion of a shunt (Yes = 1; No = 2)

```
. tab Haemorrhage
```

Haemorrhage	Freq.	Percent	Cum.
1	4	30.77	30.77
2	9	69.23	100.00
Total	13	100.00	

Developed a haemorrhage post-operatively (Yes = 1; No = 2)

```
. tab Headache
```

Headache	Freq.	Percent	Cum.
1	9	69.23	69.23
2	4	30.77	100.00
Total	13	100.00	

Pre-operative headache (Yes = 1; No = 2)

```
. tab ITUadmin
```

ITU admin	Freq.	Percent	Cum.
1	4	30.77	30.77
2	9	69.23	100.00
Total	13	100.00	

Requiring admission to intensive care post-operatively (Yes = 1; No = 2)

```
. tab Nausea
```

Nausea	Freq.	Percent	Cum.
1	7	53.85	53.85
2	6	46.15	100.00
Total	13	100.00	

Pre-operative nausea (Yes = 1; No = 2)

```
. tab Vomitting
```

Vomitting	Freq.	Percent	Cum.
1	5	38.46	38.46
2	8	61.54	100.00
Total	13	100.00	

Pre-operative vomiting (Yes = 1; No = 2)

```
. tab VisualDisturbance
```

Visual Disturbance	Freq.	Percent	Cum.
1	5	38.46	38.46
2	8	61.54	100.00
Total	13	100.00	

Pre-operative visual disturbance (Yes = 1; No = 2)

```
. tab Dizziness
```

Dizziness	Freq.	Percent	Cum.
1	7	53.85	53.85
2	6	46.15	100.00
Total	13	100.00	

Pre-operative dizziness (Yes = 1; No = 2)

```
. tab Vertigo
```

Vertigo	Freq.	Percent	Cum.
1	2	15.38	15.38
2	11	84.62	100.00
Total	13	100.00	

Pre-operative vertigo (Yes= 1; No = 2)

```
. tab Tinnitus
```

Tinnitus	Freq.	Percent	Cum.
1	1	7.69	7.69
2	12	92.31	100.00
Total	13	100.00	

Pre-operative tinnitus (Yes = 1; No =2)

```
. tab Oscillopsia
```

Oscillopsia	Freq.	Percent	Cum.
2	13	100.00	100.00
Total	13	100.00	

Pre-operative oscillopsia (Yes = 1; No = 2)

```
. tab Mobilityaid
```

Mobility aid	Freq.	Percent	Cum.
1	1	7.69	7.69
2	12	92.31	100.00
Total	13	100.00	

Mobility aid use pre-morbid (Yes = 1; No = 2)

```
. tab Aidtype
```

Aid type	Freq.	Percent	Cum.
2	1	7.69	7.69
5	12	92.31	100.00
Total	13	100.00	

Type of aid use

Type of mobility aid	Walking stick	Walking stick = 1
	Zimmer frame	Zimmer frame = 2
	1 crutch	1 crutch = 3
	2 crutches	2 crutches = 4
	Independent	Independent = 5

Type of mobility aid used pre-morbid. Data taken from Excel codebook

```
. sum ET_TP1_Comp ET_TP2_Comp ET_TP3_Comp
```

Variable	Obs	Mean	Std. Dev.	Min	Max
ET_TP1_Comp	13	58.69231	16.22439	34	83
ET_TP2_Comp	9	61.33333	11.04536	49	86
ET_TP3_Comp	8	68.125	18.79542	29	85

.

Equitest data for Time points one, two and three

```
. sum ET_Cond5_T1_Av ET_Cond5_T2_Av ET_Cond5_T3_Av
```

Variable	Obs	Mean	Std. Dev.	Min	Max
ET_C~5_T1_Av	13	25.84615	27.60992	0	64
ET_C~5_T2_Av	9	20	18.70829	0	47
ET_C~5_T3_Av	8	44.5	30.21353	0	71

Average score on condition five of SOT at timepoint one, two and three

```
. sum NoFalls_Cond5_T1 NoFalls_Cond5_T2 NoFalls_Cond5_T3
```

Variable	Obs	Mean	Std. Dev.	Min	Max
NoFalls~5_T1	13	1.615385	1.445595	0	3
NoFalls~5_T2	9	1.555556	1.236033	0	3
NoFalls~5_T3	8	.875	1.356203	0	3

Average number of falls on condition five of the SOT at time-point one, two and three

```
. sum ET_Cond6_T1_Av ET_Cond6_T2_Av ET_Cond6_T3_Av
```

Variable	Obs	Mean	Std. Dev.	Min	Max
ET_C~6_T1_Av	13	35.69231	26.85574	0	82
ET_C~6_T2_Av	9	39.33333	30.28614	0	85
ET_C~6_T3_Av	8	45	31.59114	0	81

Average score on condition six of SOT at timepoint one, two and three

```
. sum NoFalls_Cond6_T1 NoFalls_Cond6_T2 NoFalls_Cond6_T3
```

Variable	Obs	Mean	Std. Dev.	Min	Max
NoFalls~6_T1	13	1.153846	1.281025	0	3
NoFalls~6_T2	9	1.111111	1.269296	0	3
NoFalls~6_T3	8	1	1.309307	0	3

Average number of falls on condition six of the SOT at time-point one, two and three

```
. sum ET_TP1_Comp ET_TP2_Comp ET_TP3_Comp
```

Variable	Obs	Mean	Std. Dev.	Min	Max
ET_TP1_Comp	10	54.1	15.70173	34	83
ET_TP2_Comp	8	61.875	11.6795	49	86
ET_TP3_Comp	7	66.57143	19.73877	29	85

Equitest data for T1, T2 and T3 for cerebellar tumour participants

```
. sum ET_TP1_Comp ET_TP2_Comp ET_TP3_Comp
```

Variable	Obs	Mean	Std. Dev.	Min	Max
ET_TP1_Comp	6	61.33333	17.82882	42	83
ET_TP2_Comp	6	61.83333	12.70302	49	86
ET_TP3_Comp	6	73.16667	11.92337	52	85

SOT composite data for participants with complete SOT data sets

Variable	Obs	Mean	Std. Dev.	Min	Max
GaitSpeed_..	13	1.31	.2632806	.87	1.66
GaitSpeed_..	9	.9866667	.4348563	.31	1.58
GaitSpeed_..	8	1.30375	.2325595	.84	1.56

Preferred Gait Speed at time-points one, two and three

```
. sum GaitSpeed_T1_Maxmsec GaitSpeed_T2_Maxmsec GaitSpeed_T3_Maxmsec
```

Variable	Obs	Mean	Std. Dev.	Min	Max
Ga~1_Maxmsec	13	1.716923	.3878441	1.25	2.7
Ga~2_Maxmsec	9	1.193333	.415602	.4	1.74
Ga~3_Maxmsec	8	1.53	.2807134	1.09	1.84

Data for maximum walking speed

```
. sum GaitSpeed_T1_HTmsec GaitSpeed_T2_HTmsec GaitSpeed_T3_HTmsec
```

Variable	Obs	Mean	Std. Dev.	Min	Max
Gai~1_HTmsec	13	1.33	.3115017	.71	1.7
Gai~2_HTmsec	9	.9455556	.3872696	.26	1.5
Gai~3_HTmsec	8	1.11125	.5479165	0	1.7

Walking speeds with head turns

```
. sum NHPT_1_R_secs NHPT_2_R_secs NHPT_3_R_secs
```

Variable	Obs	Mean	Std. Dev.	Min	Max
NHPT_1_R_s~s	13	24.34692	13.65915	15.33	68
NHPT_2_R_s~s	9	23.35889	4.18765	16.09	30.88
NHPT_3_R_s~s	8	24.30125	14.46148	14.94	59.26

Nine Home Peg Test Data for the right upper limb

```
. sum NHPT_1_L_secs NHPT_2_L_secs NHPT_3_L_secs
```

Variable	Obs	Mean	Std. Dev.	Min	Max
NHPT_1_L_s~s	13	28.24923	21.03876	16.63	97
NHPT_2_L_s~s	9	25.46222	5.64226	18.23	34.69
NHPT_3_L_s~s	8	25.9075	12.31766	16.31	52.45

Nine Hole Peg Test Data for Left upper limb

```
. sum NHPT_1_R_secs NHPT_2_R_secs NHPT_3_R_secs
```

Variable	Obs	Mean	Std. Dev.	Min	Max
NHPT_1_R_s~s	10	25.58	15.50255	15.33	68
NHPT_2_R_s~s	8	23.065	4.37644	16.09	30.88
NHPT_3_R_s~s	7	24.98429	15.48017	14.94	59.26

Summary statistics for NHPT, for participants with cerebellar tumours

```
. sum Age
```

Variable	Obs	Mean	Std. Dev.	Min	Max
Age	10	54	13.35831	34	77

Summary statistics of age in participants with cerebellar tumours

```
. sum DHI_Comp_1 DHI_Comp_2 DHI_Comp_3 DHI_Comp_4
```

Variable	Obs	Mean	Std. Dev.	Min	Max
DHI_Comp_1	13	21.23077	22.88432	0	68
DHI_Comp_2	9	32.22222	30.0906	0	72
DHI_Comp_3	8	24.25	28.93219	0	64
DHI_Comp_4	7	25.14286	26.57962	0	58

Dizziness Handicap Inventory

```
. sum Box_2 Box_3 Box_4
```

Variable	Obs	Mean	Std. Dev.	Min	Max
Box_2	10	3.1	2.601282	0	8
Box_3	8	.25	.7071068	0	2
Box_4	8	.5	1.069045	0	3

Box scale for Pain

```
. sum Box_2 Box_3 Box_4
```

Variable	Obs	Mean	Std. Dev.	Min	Max
Box_2	5	1.6	2.073644	0	5
Box_3	5	.4	.8944272	0	2
Box_4	5	.6	1.341641	0	3

Summary statistics for 5 participants with complete data sets for box scale for pain

```
. sum LASA_1_1OverallQOL LASA_2_1MentalIntellectual LASA_31Physical LASA_4_1Emotional LASA_6_1Spirit
```

Variable	Obs	Mean	Std. Dev.	Min	Max
LASA_1_1Ov~L	12	7.333333	2.534609	2	10
LASA_2_1Me~l	12	7.75	2.137331	4	10
LASA_31Phy~l	12	7.916667	2.391589	3	10
LASA_4_1Em~l	12	7.333333	1.61433	4	10
LASA_6_1Sp~l	12	8.333333	2.424621	2	10

LASA quality of life measure for overall QOL, mental, physical, emotional and spiritual wellbeing at time-point one, preoperatively

```
. sum LASA_1_1OverallQOL LASA_2_1MentalIntellectual LASA_31Physical LASA_4_1Emotional LASA_6_1Spirit
```

Variable	Obs	Mean	Std. Dev.	Min	Max
LASA_1_1Ov~L	5	8.8	1.30384	7	10
LASA_2_1Me~l	5	9	1.414214	7	10
LASA_31Phy~l	5	8.8	1.788854	6	10
LASA_4_1Em~l	5	8.4	1.140175	7	10
LASA_6_1Sp~l	5	9.2	1.30384	7	10

Summary statistics for 5 participants with complete data sets for overall QOL, mental, physical, emotional and spiritual wellbeing at T1, preoperatively

```
sum LASA_1_4OverallQOL LASA_2_4Mental LASA_3_4Physical LASA_4_4Emotional LASA_6_4Spiritual
```

Variable	Obs	Mean	Std. Dev.	Min	Max
LASA_1_4Ov~L	8	7.125	2.167124	4	10
LASA_2_4Me~l	8	7.875	1.95941	5	10
LASA_3_4Ph~l	8	6.875	2.531939	3	10
LASA_4_4Em~l	8	7.25	1.38873	6	10
LASA_6_4Sp~l	8	8.25	1.581139	6	10

LASA quality of life measure for overall QOL, mental, physical, emotional and spiritual wellbeing at time-point four, 6 months post-operatively

```
. sum LASA_1_4OverallQOL LASA_2_4Mental LASA_3_4Physical LASA_4_4Emotional LASA_6_4Spiritual
```

Variable	Obs	Mean	Std. Dev.	Min	Max
LASA_1_4Ov~L	5	7.2	1.923538	5	10
LASA_2_4Me~l	5	8.2	2.48998	5	10
LASA_3_4Ph~l	5	7	2.236068	4	10
LASA_4_4Em~l	5	7.2	1.788854	6	10
LASA_6_4Sp~l	5	8.6	1.341641	7	10

Summary statistics for 5 participants with complete data sets for overall QOL, mental, physical, emotional and spiritual wellbeing at T4, postoperatively

```
. sum InptDays
```

Variable	Obs	Mean	Std. Dev.	Min	Max
InptDays	13	19.76923	21.59149	5	81

Duration of Inpatient stay

```
. tab ReasonforExclusion
```

Reason for Exclusion	Freq.	Percent	Cum.
1	4	12.90	12.90
2	8	25.81	38.71
3	2	6.45	45.16
4	8	25.81	70.97
5	1	3.23	74.19
6	3	9.68	83.87
7	2	6.45	90.32
8	3	9.68	100.00
Total	31	100.00	

Excluded participants

Codebook for Excluded Participants			
Unable to consent = 1			
Previous Cerebral Surgery = 2			
Not identified prior to Surgical intercvention = 3			
Emergency transfer = 4			
Previous RTX = 5			
Unable to stand for 20 seconds = 6			
Refusal to participate = 7			
Did not have a surgical intervention = 8			

Coding structure for excluded participants taken from Excel codebook